# Early Visual Contributions to Reading

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## Declaration

I, John Hogan, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

## General Abstract

Reading requires integrating visual and linguistic processes, so it is perhaps surprising that models of visual word recognition focus almost entirely on language, to the exclusion of vision. Neurological models of reading assume that visual information proceeds serially from the retina through the early visual cortices, where a hierarchy of increasingly complex feature detectors transform the sensory-bound retinotopic code into progressively more abstract forms, eventually reaching reading-specialised populations that encode orthographic units. These orthographic detectors are *the* input pathway to the wider language system. This notion of a serial staged hierarchy culminating in abstract detectors, however, is likely overly simplistic accumulating. Evidence suggests that the occipitotemporal system is better understood as a highly recurrent network. Classical hierarchical accounts and interactive processing models make contrasting predictions about how early visual areas contribute to reading. To test these predictions, I retinotopically mapped occipital visual areas and then measured (fMRI) their neural response to different reading tasks. I found that reading strongly engaged areas V1-V3 bilaterally, both in the central (stimulated) regions and in regions coding the periphery, suggesting both bottom-up and top-down influences in early visual cortices. Within the central regions of V1-V3, activity was significantly stronger for low frequency than high frequency words, again suggesting that non-visual factors such as lexical frequency influence processing in the earliest visual areas. Subsequent analyses revealed that ventral (V4, VO-1, VO-2) and dorsal (V3a, V3b, V7) regions were both active during reading, with no evidence of any difference in the strength of activation between them. Lastly, I found that a seemingly incidental property of the experimental paradigm (stimulus presentation rate) dramatically affected V1-V3 activity.

Together these results contradict the notion that the early visual stages of reading are tightly sensory-bound and require reading-specific neuronal representations. Rather, these findings suggest that reading is an interactive process, even in the earliest visual cortices.

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# *1. General Introduction*

## 1.1. Reading

Reading is visually demanding. Consider the difference between “acre” and “acne”. English literates are unlikely to mistake the two but visually the difference is slight; just extend the of the arc of the “r” down vertically and it becomes an “n”. This subtle difference, however, dramatically effects both the meaning and the sound of the words; one is a unit of land measurement while the other is a common skin condition. Furthermore, the two words do not even sound similar as they share only a single phoneme, namely the [k] in [ā-kər] and [ak-nē]. This type of subtle, but crucial, visual distinction is a common feature of all written languages, including alphabetic, syllabic, and logographic scripts (see Figure 1).

| **Alphabetic** *Arabic* | | **Syllabic** *Hindi* | | **Logographic** *Mandarin* | |
|---|---|---|---|---|---|
| رمان pomegranate | زمان time/era | आज today | आजा come | 夫 man | 天 sky |
| نعم yes | نغم melody | खेत field | खत letter | 入 enter | 人 human |
| مغلوب defeated | مقلوب turned over | काल time | कील nail | 我 me | 找 find |

*Figure 1. In writing systems, subtle visual form differences can be critical for correctly identifying words. Above are examples from alphabetic (Arabic), syllabic (Hindi), and logographic (Mandarin) orthographies. Literacy in a language makes recognizing these visual differences quick and effortless. In contrast, identifying these differences in an unfamiliar script typically involves conscious serial comparisons.*

Writing systems encode spoken language and learning to read requires learning to associate the spatial forms of a writing system with corresponding sound and meaning. With training, the brain becomes remarkably proficient at making these associations. A typical English adult reader can read hundreds of words per minute and can easily deal with the wide

variation in surface form found in everyday writing (e.g. *Script*, CASE, size). How the literate brain makes these associations so rapidly and effectively is still not well understood.

We do know that within the fraction of the second it takes the brain to recognise a visually presented word, light (photons) from the word stimulus was transduced into neural impulses in the retina; the spatial information was transmitted along visual pathways to the neocortex; and a cascade of activity spread through the occipital, temporal, parietal and frontal systems that eventually produced the linguistic judgement. How exactly the neural circuits of the brain link the sensory-bound spatial input with the non-spatial phonological, semantic, articulatory, and other related codes is a central question in cognitive neuroscience.

Whatever the solution, it is implemented on a neural substrate without a pre-specialisation for written language. Literacy has only become wide-spread in the human population over the last few hundred years and there has simply not been sufficient time for evolution to tailor structures of the brain specifically to reading. Unsurprisingly then, written language, unlike spoken and signed language[1], does not develop naturally in children and requires years of explicit training to master.

Perhaps revealing, a child's proficiency with spoken language is a key factor in how quickly and effectively they acquire written language. Phonemic awareness, namely the ability to identify the phonological units within a word (e.g. rimes or syllables), is among the strongest

[1] While there are some differences, spoken and manual communication have many similar properties and depend on more or less the same brain regions. Hereafter in this thesis, references to "language" refers to both spoken and sign language.

predictors of reading achievement across cultures (Goswami, 1999; Ziegler & Goswami, 2005) suggesting that learning reading requires tapping into existing spoken language systems.

According to a prominent neurological model of reading (Dehaene, Cohen, Sigman, & Vinckier, 2005), integrating visual and linguistic forms requires "recycling" neurons in the visual system into reading-specialised detectors that encode abstract orthographic forms that can be linked to phonological, semantic, and other linguistic codes in the perisylvian regions and beyond. Whether reading requires specialised orthographic detectors, however, is a topic of ongoing debate (Dehaene & Cohen, 2011; Price & Devlin, 2011) and is one of the central questions examined in this thesis.

## 1.2. Cortical areas involved in reading

In 1988 researchers saw the first images of brain activity during reading. In a landmark study, Petersen and colleagues (1988) used positron emission tomography (PET) to measure changes in regional blood flow, a correlate of neural activity, while subjects heard auditory words and read visually presented words (all frequent English nouns). Relative to fixation, visual words strongly activated bilateral striate and extrastriate cortices extending anteriorily to the temporal-occipital boundary. Auditory words, in contrast, most strongly activated the bilateral primary auditory cortex along with left-lateralised activity in the temporoparietal cortex, anterior superior temporal cortex, and inferior anterior cingulate cortex. To isolate amodal activity, speech production and semantic association tasks were

used. These tasks elicited strong responses in inferior frontal gyrus (i.e. Broca's area), the supplementary motor area (SMA), and the cerebellum. Overall, the brain activity showed that written and spoken language, while engaging different sensory systems (visual and auditory cortices respectively), rely on a largely overlapping network for meaning and speech processes. Remarkably, this early neuroimaging investigation identified all three cortical territories that are now known to be critical for reading: (i) areas of the occitpito-temporal cortex involved in visual processing; (ii) temporo-parietal areas involved in processing the sounds of words; and (iii) inferior frontal areas involved in articulation (Price, 2012; Pugh et al., 2000).

The inferior frontal lobe's critical role in speech production was first identified by Pierre Paul Broca (1861a, 1861b, 1865). He saw a patient, Monsieur Lebourgne, who was unable to produce speech beyond the syllable "tan" but who could understand speech and was able to follow directions and move his articulators well. He died soon after Broca's visit and at autopsy there "was a large cavity, capable of holding a chicken egg" in the posterior portion of the inferior frontal gyrus (1861a, p. 236). Broca concluded that this was the cortical site of articulated speech (i.e. speech production) and now this eponymous region is considered a classic 'language area' in the brain.

The second classic 'language area' was identified by Karl Wernicke (1874) when he studied two patients with language comprehension deficits. Both were able to fluently produce speech although it was full of neologisms and largely empty of content. Both patients had lesions around the temporo-parietal junction. Based on these two patients, Wernicke (1874) proposed the first neurological model of language. In brief, spoken language input enters

what is now called Wernicke's area where the auditory signal is recognised as a series of words. To speak, these auditory word forms linked via the arcuate fasiculus to the motor word patterns stored in Broca'a area.

In 1892, the French neurologist Joseph Dejerine extended Wernicke's (1874) neurological model of spoken language to include reading. Dejerine based the model on his observations of two patients. His first patient was a 63 year old sailor who suddenly became unable to read or write (Dejerine, 1891). A post-mortem revealed an extensive lesion that included the left angular gyrus. Dejerine reasoned that the patient was unable to read or write (*alexia with agraphia*) because he lost the cortical representation of visual word forms, which he argued were stored in the angular gyrus. The second patient also suddenly lost the ability to read letters and words but could still write (*alexia without agraphia*). After a short break however, the patient could not read what he had just written. Shortly before dying, this patient suddenly became unable to write. Consistent with the recent change in symptomatology, Dejerine found evidence of both new and older lesions at post-mortem. The older damage included a left hemisphere occipital infarct that extended through the lingual lobe, fusiform, cuneus, and splenium of the corpus callosum. The more recent damage was localised around inferior parietal lobe and included extensive damage to the angular gyrus. Considered together, the anatomic evidence from these two patients showed that damage to the angular gyrus disrupts both reading and writing ability while damage limited to just the occipital-temporal region, like the second patient had until shortly before his death, disrupts only reading and spares writing ability.

According to Dejerine's model (1892, see Figure 2), the left angular gyrus stores the visual word codes needed to link with the phonological forms in Wernicke's area that are used for writing and comprehension. The visual word forms in the angular gyrus, according to Dejerine (1892), develop following extensive exposure to visual word input conveyed by the left and right visual cortices. In 'pure alexia' (*alexia without agraphia*) the word forms in the angular gyrus are intact, they just cannot be accessed because the pathways between the visual system and the angular gyrus have been severed. Writing ability, however, is spared because the visual word forms in the angular gyrus still have an intact pathway to the auditory word forms in Wernicke's area and then to the motor forms in Broca's area that enable writing. Of course, a pure alexic cannot read what they have just written because the pathway linking visual input to word forms in the angular gyrus is severed. This 'classical' neurological interpretation of pure alexia as a disconnection syndrome (severing the visual input from the bilateral visual system from visual word forms in the left angular gyrus) remains influential.

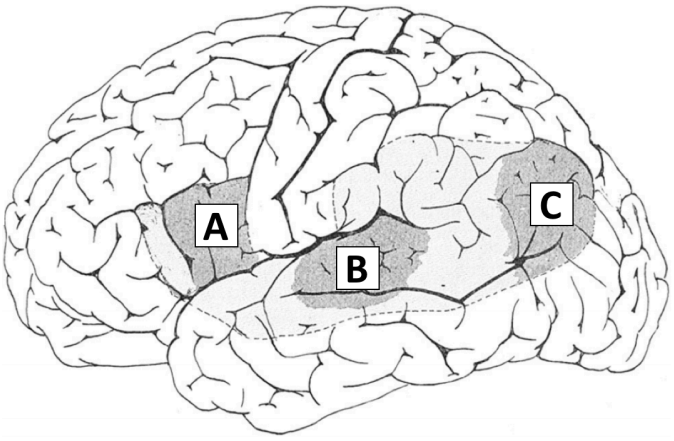



*Figure 2. Dejerine's language model (adapted from Dejerine & Dejerine-Klumpke, 1895, p. 247; and Krestel, Annoni, & Jagella, 2013). (A) Broca's area stored the motor forms of words needed for written and spoken output. (B) Wernicke´s area stored the auditory forms for words needed for processing speech sounds and when generating internal speech. (C) The visual word area stored the visual forms of words needed to link visual input from the occipital lobes with the auditory and motor in Wernicke's and Broca's area respectively.*

The classical neurological model of reading has a number of important shortcomings including: (i) it is strongly left lateralized (Broca, 1865; Dejerine, 1891; Wernicke, 1874)

whereas more modern models are less committed to that notion; (ii) the functions ascribed to each region are now considered to be either more complex, or simply different, than the original explanations; and (iii) by focusing on three cortical territories (Broca's area, Wernicke's area and the angular gyrus), key anatomical regions were missed including the supramarginal gyrus and ventral occipito-temporal cortex.

Classical models focus on left hemisphere because the patients that provided the evidence for the models all had left-hemisphere damage (Broca, 1865; Dejerine, 1891; Wernicke, 1874). Even at the time, however, the accuracy of these lesion-deficit characterizations was questioned (Marie, 1906). More recently, cases of crossed aphasia (Assal, Perentes, & Deruaz, 1981; Carr, Jacobson, & Boller, 1981; Castro-Caldas & Confraria, 1984; Croquelois & Bogousslavsky, 2011; Henderson, 1983; Puel et al., 1982; Yarnell, 1981) suggest that in some people at least, the right hemisphere plays an important role in language processing. It is possible that these patients simply represent the small portion of the normal population with either bilateral or right-dominant language function (Binder et al., 1996; Knecht et al., 2000; Knecht et al., 2002; Penfield & Roberts, 1959) although there is growing evidence that core language functions rely on both hemispheres to a greater extent than previously suspected. For example, Hartwigsen et al. (2010) showed that stimulating either the left or right supramarginal gyrus interferes with making phonological decisions on words. Similarly, in their extensive review of semantic processing, Binder et al. (2009) found that most neuroimaging studies report bilateral activation for semantic processing. In other words, the extent that core language functions are lateralised is unclear and even if a function is left-dominant in most people, the degree to which the right hemisphere contributes to that function is an open question.

A second issue with the classical model is the functions ascribed to individual brain regions. We know now, for example, that Broca's area is not limited to speech production but is also involved in language comprehension. Buckner et al. (1995) and Fiez (1997) observed that many functional neuroimaging studies of word comprehension show activations in Broca's area. Moreover, they noted that those studies focused on word meaning (i.e. semantics) show activation in more anterior and ventral parts of Broca's area *(*pars triangularis and pars orbitalis) while those focusing on the sounds of words (i.e. phonology) activate more posterior and dorsal parts of Broca's area (pars opercularis and ventral premotor cortex). Using transcranial magnetic stimulation (TMS), Gough and colleagues (2005) confirmed this anterior-posterior functional division and showed that the temporary disruption of anterior Broca's area selectively interfered with semantic processing while stimulation to posterior Broca's area selectively interfered with phonological processing. Further, studies directly comparing reading and listening of narratives show that both of those tasks activate Broca's area (Spitsyna, Warren, Scott, Turkheimer, & Wise, 2006), suggesting the region responds strongly to language independent of the modality. In summary, both the function of Broca's area and the anatomical boundaries relevant to reading, and language more generally, are different from Broca's (1861a, 1861b, 1865) original proposals.

Although the precise anatomical definition of Wernicke's area continues to be debated (Binder, 2015; Bogen & Bogen, 1976), it is clear that in addition to the posterior superior temporal gyrus (i.e. auditory association cortex), large parts of the inferior parietal lobe (IPL) are involved in language processing (Binder et al., 2009; Hartwigsen, Golombek, & Obleser, 2015). In the IPL, the anterior and posterior ends also seem to perform different functions.

The anterior segment of the IPL (supramarginal gyrus) plays an important role in both phonological processing (Booth et al., 2004; Petersen et al., 1988; Raizada & Poldrack, 2007; Seghier et al., 2004; Yoncheva, Zevin, Maurer, & McCandliss, 2010; Zevin & McCandliss, 2005) and verbal working memory (Romero, Walsh, & Papagno, 2006) and is linked to the posterior part of Broca's area via the third branch of the superior longitudinal fasciculus (Petrides & Pandya, 1984, 2009) . Together the posterior part of Broca's area and the supramarginal gyrus jointly contribute to phonological processing and verbal working memory (Buchsbaum & D'Esposito, 2008; Pattamadilok, Knierim, Kawabata Duncan, & Devlin, 2010). In contrast, the posterior half of the IPL (angular gyrus) is an important node in a network of regions involved in semantic processing, that also includes anterior parts of Broca's area (Binder et al., 2009). The angular gyrus sits at the posterior end of the inferior longitudinal fasciculus which runs along the temporal lobe, linking with the middle temporal gyrus and anterior temporal poles. The temporal poles, in turn, link to anterior parts of Broca's area via the uncinate fasciculus (Anwander, Tittgemeyer, von Cramon, Friederici, & Knosche, 2007).

Based on these and other findings, modern neuroanatomical models of spoken language have moved beyond the classical circuit linking Broca's and Wernicke's areas and now incorporate a more extensive set of neuroanatomical regions (Tremblay & Dick, 2016), that at a minimum includes two separate fronto-parietal circuits (see Figure 3): (i) the posterior parts of Broca's area and the supramarginal gyrus that preferentially contribute to phonological processing; and (ii) more anterior and ventral parts of Broca's area and the angular gyrus that preferentially contribute to semantic processing. Both circuits are

considered to function independently of the modality of the input and thus are not limited to spoken or written words.

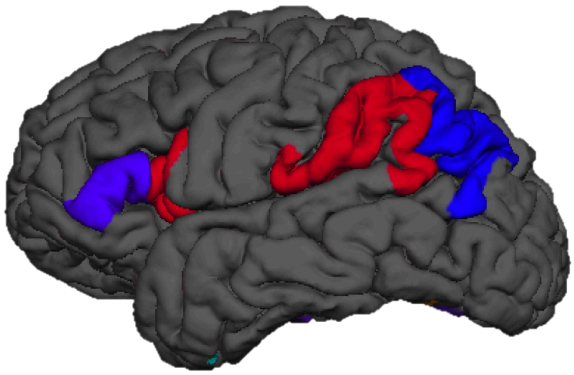


*Figure 3. Fronto-parietal language circuits. Most modern neurological models of language include two separate fronto-parietal circuits: (i) the posterior aspect of Broca's area and the supramarginal gyrus (shown in red); and (ii) the anteroventral aspects of Broca's area and the angular gyrus (shown in blue). These circuits are thought to preferentially contribute to phonological and semantic processing, respectively. The fronto-parietal areas are shown on one participant's left hemisphere surface (created using Freesurfer, see section 2.5 of General Methods for more information) according to the coordinates in Freesurfer's Desikan-Killiany Atlas.*

Finally, an important limitation of the classic neurological model of reading is that it does not include the ventral occipito-temporal (vOT) cortex (see Figure 4). Virtually all modern studies of reading demonstrate that vOT is engaged by visual words (Cohen et al., 2000; Fiez & Petersen, 1998; Nobre, Allison, & McCarthy, 1994; Price et al., 1994; Pugh et al., 2001; Rumsey et al., 1997; Shaywitz et al., 2004) but the region was missing from earlier accounts, despite indications it was important as early as 1892 (Dejerine, 1892).

## 1.3. Ventral occipito-temporal cortex and the reading-specialisation hypothesis

Cohen and colleagues (2000) used modern fMRI and electroencephalography (EEG) techniques to test the classical prediction (Dejerine, 1892; Geschwind, 1965) that reading depends on visual information in the occipital lobe reaching critical structures in the left hemisphere. To test this prediction, the researchers compared brain activity in two patients

with posterior callosal lesions against five control subjects as both groups read words and non-words shown (alternatingly) in their left and right hemifields. As expected, in both groups the neural response to split-hemifield reading included early activity in the occipital lobe that was stronger in the contralateral than ipsilateral hemisphere. In controls, however, left vOT responded more strongly than the right vOT regardless of the hemifield the words were shown in. Furthermore, event-related electrical activity recorded by the left inferior temporal (IT) electrodes suggested that left vOT was also sensitive to the differences between words and non-words (i.e. strings of consonants). This early "lexicality signature" (180-200ms) was also seen in one of the patients, but crucially only for right hemifield words. For words shown in the left hemifield, where the patient's reading performance was found to be severely deficient, left vOT responded weakly – presumably because the patient's collosal lesion prevented the initial activity in right occipital lobe from crossing-over to the left hemisphere. Thus, as the classical model predicts, successful reading did depend on occipital activity connecting with structures in the left hemisphere. However, as seen in the controls, left vOT responds very early during reading, regardless of where the words are shown, and is sensitive to the difference between lexically valid and lexically-invalid arrangements of letters. This early, location-invariant response led the researchers to propose that left vOT, rather than temporal-parietal structures, contains the visual word form system. As the researchers noted, temporal-parietal structures also responded strongly during successful reading trials but they argued against this region being the cerebral basis for the visual words because: (i) the temporal-parietal region responds to linguistic tasks that do not involve reading (Chee, O'Craven, Bergida, Rosen, & Savoy, 1999; Price, Wise, et al., 1996); and (ii) the temporal-parietal region is not within the critical lesion

site that causes pure alexia (Beversdorf, Ratcliffe, Rhodes, & Reeves, 1997; Binder & Mohr, 1992; Cohen & Dehaene, 1995; Damasio & Damasio, 1983; Dejerine, 1892).

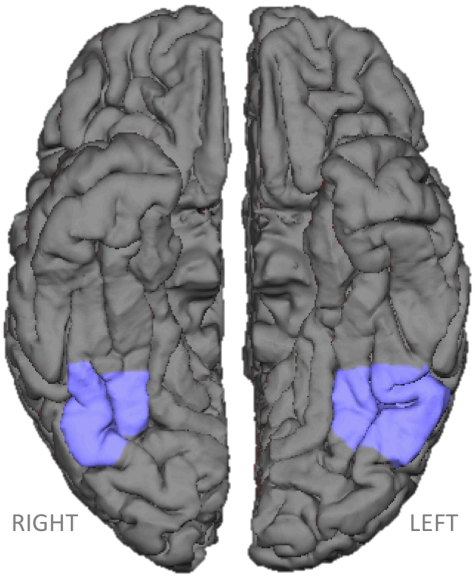



*Figure 4. The ventral occipital temporal cortex (vOT). The left and right vOT shown on the ventral aspect of one participant's left and right hemisphere surfaces. vOT was defined in both hemispheres using standard space coordinates (Twomey, Kawabata Duncan, Price, & Devlin, 2011).*

The same group of researchers began looking into how this region, that they called the "visual word form area (VWFA)," responds to different reading related demands. There were a number of notable findings. First, the VWFA is primed just as strongly by different-case (RADIO-radio) subliminal primes as by same-case (radio-radio) subliminal primes (Dehaene et al., 2001) indicating an invariance to the different surface forms of letters and words. The response in early visual areas, in contrast, was not case-invariant and priming depends on the prime–target pairs being the same case (Dehaene et al., 2001). Second, the VWFA responded just as strongly to pseudowords as to words (Cohen et al., 2002) indicating that the region is sensitive to sub-lexical orthographic properties and not just lexically valid arrangements of letters. Third and finally, the VWFA responded exclusively to written but not spoken word stimuli (Dehaene, Le Clec, Poline, Le Bihan, & Cohen, 2002) suggesting that the region plays a unimodal visual role in recognizing words. This evidence, Dehaene and

Cohen (2004) argued, strongly supports their hypothesis that left vOT contains orthographically specialized visual detectors.

Dehaene and Cohen (2004), however, note an apparent paradox: functionally defined, the VWFA shows up in consistent location across individuals (c.f. Cohen & Dehaene, 2004) but written language is far too evolutionarily recent for there to be a genetically specialized region dedicated to it. Dehaene et al.'s (2005) Local Combination Detector (LCD) model provided some preliminary answers. Electrophysiological studies in non-human primates show that within only a few training trials, neurons in the inferotemporal (IT) cortex become attuned to detecting complex (formerly) novel objects (Logothetis & Pauls, 1995). According to their LCD model, the plasticity of IT neurons and the extreme exposure to written words when learning to read 're-cycles' neurons into dedicated orthographic detectors. This recycling recruits a similarly located population of neurons across individuals because those neurons are situated at just the right point in the visual system where (mostly) innate factors have created receptive fields that are large and complex enough to meet the spatial demands of writing systems. The LCD model is based on hierarchical frameworks developed from electrophysiology studies in non-human primates (e.g. Riesenhuber & Poggio, 1999; Rolls, 2000) and details how an essentially feedforward network of converging neural detectors in the bilateral early visual areas (V1, V2, V4) culminates in left-lateralised n-gram detectors in left vOT (see Figure 5).

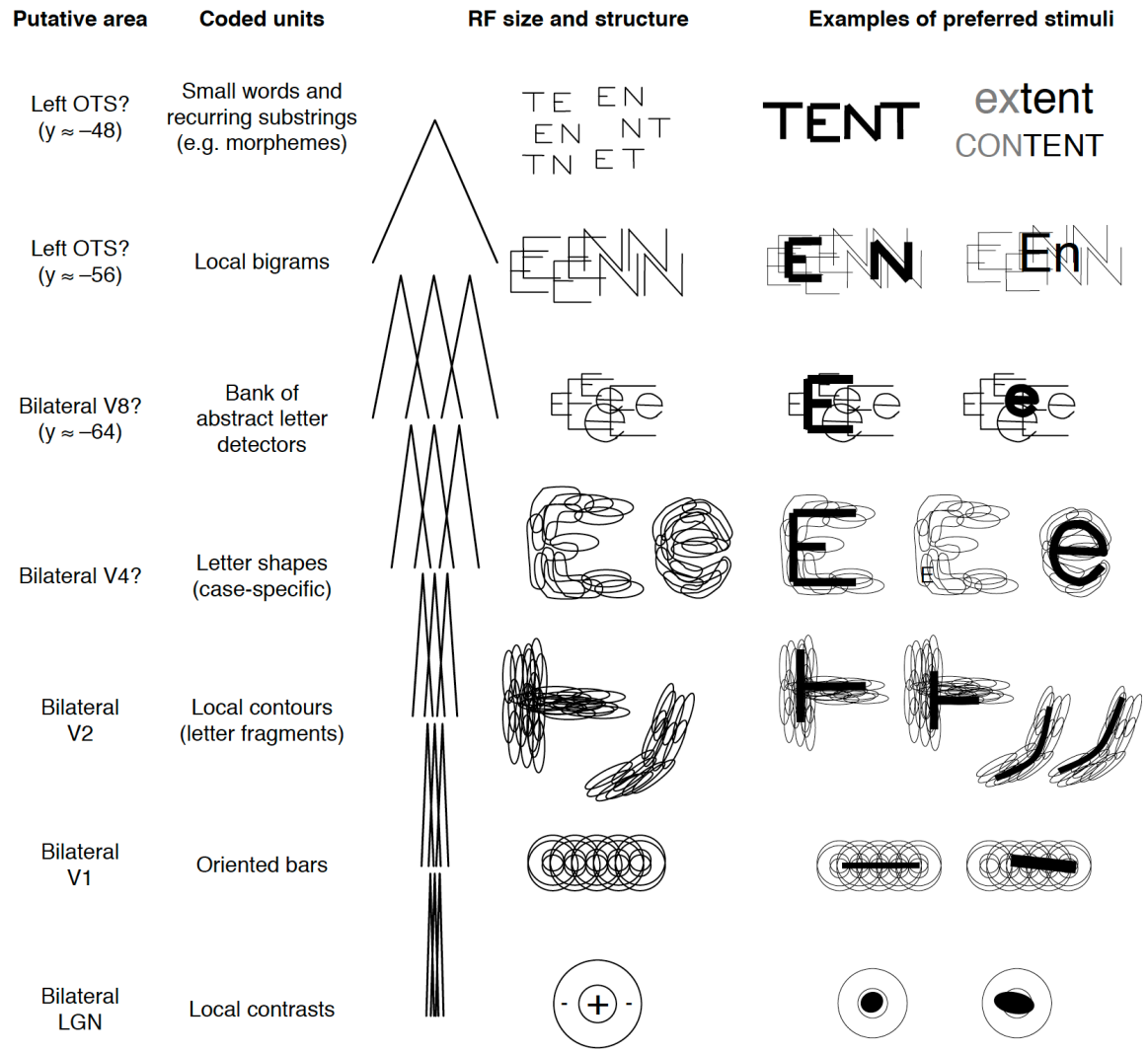



*Figure 5. The local combination detectors (LCDs) model of visual word recognition (figure from Dehaene et al., 2005). The LCD model is inspired by neurophysiological models of invariant object recognition. Neurons from lower levels converge on neurons in higher levels creating increasing large and complex receptive fields. This essential feedforward process culminates in invariant letter, bigram, n-gram, and word detectors. Input from the earlier visual areas (V1, V2, V4) must be recoded into orthographic forms by these detectors in order to link with the linguistic representations elsewhere in the brain (Dehaene et al., 2005).*

The electrophysiological methods used to develop and evaluate classical hierarchical models are rarely available in humans (the only species that can read) so the evidence for and against the LCD model comes almost exclusively from neuroimaging. Among the strongest support is fMRI evidence showing that within left vOT there is a posterior-anterior gradient of increasing selectivity to words (Vinckier et al., 2007). Vinckier et al (2007) designed a hierarchical stimuli set that included 6-character strings ranging from: false fonts, infrequent

letters, frequent letters, frequent bigrams, frequent quadrigrams, and finally common words. The researchers measured brain activity while subjects viewed the stimuli and found two key findings. First, vOT (both left *and* right) responded more strongly the more word-like the stimuli was. This is consistent with the region containing a hierarchy of letter, bigram, and n-gram detectors. After all, recognizing a word (or pseudoword) entails also activating the neurons at the subordinate n-gram, bigram, and letter levels of the hierarchy. A letter string, in contrast, activates only the corresponding set of letter representations and not higher-order neurons. Second, when they subdivided the left vOT into smaller regions-of-interest based on the coordinates specified in the LCD model they found a gradient of selectivity running from the most posterior region, that responded similarly to all the different letter-string conditions, and gradually increasing in more anterior regions with the furthermost end preferring words and word-like stimuli (i.e. frequent quadrigrams). Overall, these two findings match well with LCD model predictions.

However, there is evidence that lexical manipulations affect activity in the left vOT, even when the sub-lexical properties are controlled across conditions. Using a parametric design, Kronbichler and colleagues (Kronbichler et al., 2004) created a stimulus set with five different levels of word frequency ranging from pseudowords as the least frequent to very common words as the most frequent. All five conditions, crucially, had the same number of letters, average syllable length, and bigram frequency. Using fMRI, the researchers measured brain activity as subjects viewed blocks of the different stimuli conditions and found that the response in left vOT was inversely related to word frequency. Given that lower-level properties were controlled across conditions, a lexical frequency effect contradicts the LCD model. According to the LCD model, left vOT contains only sub-lexical

detectors so if sub-lexical features are more or less the same across stimuli, a lexical property like how frequently a word is seen, should not influence processing at this putatively pre-lexical stage. The results, the researcher argue, indicate that the VWFA likely contains whole word representations. High frequency words elicit less activity, they speculated, because frequently accessed word representations are less effortful to retrieve. Infrequent words and pseudowords, on the other hand, are not as readily available and may instead co-activate several near-matching patterns resulting in overall higher BOLD signal (Kronbichler et al., 2004). Support for lexical representations also comes from fMRI evidence showing that the strength of left vOT adaptation to rapidly repeated words (BOAT–BOAT) drops dramatically when the prime–target pair differ by only a single letter (COAT–BOAT)(Glezer, Jiang, & Riesenhuber, 2009). Although the prime–target pairs still share bigrams (OA, AT), the strength of adaptation was similar to prime–target pairs with no overlapping features (FISH–BOAT).

## 1.4. Ventral occipito-temporal cortex and the interface hypothesis

There is now no doubt that left vOT plays an important role in the early stages of reading but the evidence against stored orthographic forms is at least as strong as the evidence for them. First, left vOT responds just as strongly for non-orthographic forms like pictures and line drawings as it does for letters and words (Kherif, Josse, & Price, 2011; Turkeltaub, Flowers, Lyon, & Eden, 2008; Wright et al., 2008). Moreover, in left vOT pictures can prime written words just as effectively as words do and vice-versa (Kherif et al., 2011). Second, even in cases when vOT does respond more strongly to words than pictures, that disparity

can be reduced or even abolished by changing task requirements (Starrfelt & Gerlach, 2007) indicating that its contribution is not as automatic and feedforward as VWFA accounts suggest. Third, the vOT also responds strongly to non-visual stimulation like when congenitally blind subjects read braille (Buchel, Price, Frackowiak, & Friston, 1998; Reich, Szwed, Cohen, & Amedi, 2011). In fact, poly-modal involvement is not even limited to spatial forms as vOT activity is stronger to auditory words than acoustic controls (Price, Winterburn, Giraud, Moore, & Noppeney, 2003). Fourth and finally, the neuropsychological evidence that left vOT is specialized for storing orthographic forms is not very strong. Lesions are rarely limited to just left vOT and typically also include extensive damage to occipital and other regions (Damasio & Damasio, 1983). This makes it difficult to confidently link deficits to damage. Moreover, pure alexia does *not* always include left vOT damage (Philipose et al., 2007; Warrington & Shallice, 1980) and left vOT damage does *not* always result in pure alexia (Hillis et al., 2005). Alas, even diagnosing the 'purity' of a deficit is difficult; without a more comprehensive and fine-grained understanding of the processes involved in reading it is hard to distinguish between a deficit specific to written language and one that involves dysfunction of a more general, underlying capability. For example, when stringent psychophysical tasks and data modelling methods are used to break down subject performance into more basic processing components, 'pure' alexia more closely resembles a general visual disorder involving a reduction of visual speed and apprehension span than a deficit that is specific to letters or words (Starrfelt, Habekost, & Gerlach, 2010; Starrfelt, Habekost, & Leff, 2009).

This apparently lack of selectivity, both in terms of the stimuli left vOT responds to and the deficits that result from damage suggest its neural circuits are not specialized solely for

detecting and encoding abstract orthographic forms. In fact, accounts of vOT function that are based on general models of visual processing (Price & Devlin, 2011) explain left vOT's response to words as well as the VWFA theories based on specialized sub-lexical (Cohen & Dehaene, 2004; Dehaene & Cohen, 2011; Dehaene et al., 2005; Vinckier et al., 2007) or lexical (Glezer et al., 2009; Kronbichler et al., 2004) encoding. According to the Interactive Account of ventral occipitotemporal contributions to reading (IA; Price & Devlin, 2011), reading involves the same neural mechanisms as any other form of higher order vision and diverges from the LCD account both in terms of how the bottom-up hierarchy encodes information, and, crucially, in how top-down activity contributes to the process. As in the LCD model, converging forward afferents in the early visual areas create increasingly complicated receptive fields. Unlike the LCD model, however, this feedforward hierarchy does not result in single, invariant object encoders. Rather, complex visual forms are encoded by the pattern of activity across a distributed population of neurons. Within the population, each neuron encodes spatial patterns found in the object but what they encode depends on the wider context, conveyed by both bottom-up and top-down connections, and is not fixed to any one type of object. For example, a neuron sensitive to a contour resembling an "r" may be active for written words like "tiger" but also for pictures of tigers with "r" like stripe patterns. Understanding how neurons and neural populations respond, according to the Interactive Account, involves considering top-down input. Specifically, in terms of reading, the Interactive Account argues that left vOT activity is better understood within the general neurobiological framework of predictive coding (Friston, 2010) where higher areas of the brain are seen as actively trying to predict bottom-up sensory input. In this framework, higher neural structures send predictions along feedback connections to lower neural structures in an attempt to 'explain away' the ascending sensory signal (see

Figure 6). The remaining 'error' activity propagates forward through the network. With training and exposure, the accuracy of the top-down predictions improves. Learning to read, according to the IA model, improves the predictions phonological, semantic, and other language-related systems send to vOT.

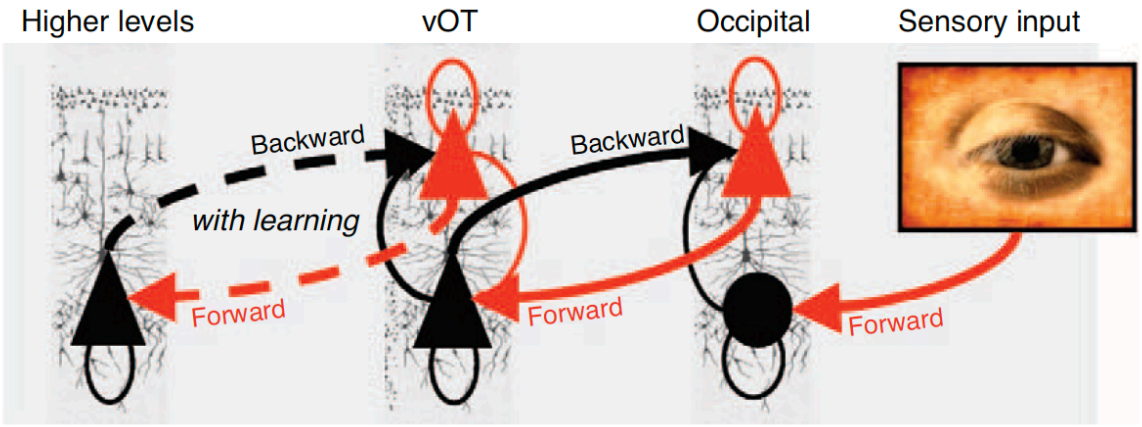



*Figure 6. A schematic of how sensory input is processed according to Interactive Account of vOT function (from Price & Devlin, 2011). Neurons in the supragranular layer send forward driving projections (red). Neurons in the infragranular layer send backward (modulatory) connections. The feedback connections transmit predictions of the forward response and the difference, or prediction error, propagates forward through the network. In a recurrent process, prediction error adjusts feedback predictions until error is minimized. Thus, the recurrent connectivity between different levels changes with experience and training (indicated as dashed lines between the vOT and higher levels).*

Differences in top-down prediction, proponents argue, provides a parsimonious account of how vOT responds during reading experiments. For example, vOT responds more weakly to high frequency words than pseudowords or low frequency words (Kronbichler et al., 2004) because high frequency words are seen more often and thus have better developed top-down predictions and ultimately smaller error signal and less overall activation. In the case of subliminal priming, vOT responds just as strongly to same-case (radio-radio) and mixed-case (RADIO-radio) primes (Dehaene et al., 2001) because the phonological and semantic associations are the same and thus both cases elicit similar top-down predictions. Similarly, words and pictures can subliminally prime each other even though they have completely different visual forms because they share common phonological and semantic associations.

What distinguishes vOT during reading is not that it encodes abstract orthographic forms or is specialized for written language but that it is situated in a neuroanatomic sweet-spot with just the right profile of bottom-up spatial input and top-down projections from circuits involved in processing sound and meaning (Price & Devlin, 2011).

The LCD and IA models make several contrasting predictions about how the early visual areas contribute to reading. The IA model considers interactivity to be ubiquitous in the brain and predicts that even the earliest sensory cortices integrate top-down information during reading. The LCD model is more restrictive. First, because left vOT is considered to be the only route for linking the sensory-encoded words in the occipital lobes with the linguistic codes in the perisylvian cortices and beyond, it is a bottleneck during reading and higher-order linguistic manipulations should not influence neural processing in preceding visual areas. Second, given this emphasis on feedforward processing, the LCD model predicts that any reading-related specialisation of receptive fields along the visual pathways will only form at retinal locations where reading most often takes place (i.e. the fovea and parafovea). Both of these stipulations and predictions will be tested in this thesis.

## 1.5. Early visual pathways

In this section, I describe the anatomy and physiology one of the key neural inputs into the cortical reading system: the retina and the retinogeniculostriate pathway. I then review the early neuroanatomical and electrophysiological evidence that formed the foundation of the classical hierarchical model of visual processing (discussed in section 1.6) on which the LCD model of word recognition (Dehaene et al., 2005) is based. In this review, I also survey more

recent evidence to highlight where classical models are incomplete, including, most prominently, their relative neglect of feedback connections. Finally, I describe how retinotopy is maintained across the synaptic stages of the retinogeniculostriate pathway. I use this retinotopic organisation to delineate the borders of my cortical regions of interest (using a fMRI retinotopic mapping technique, see sections 1.7 and General Methods).

The neural process of recognising words starts in the retina where photosensitive sensory cells (photoreceptors) transduce patterns of light into neural codes that are then sent to central structures along the retinogeniculostriate pathway and other projections. A considerable amount of visual processing takes place in the retina. From the estimated 100 million photoreceptors lining the retina (Curcio, Sloan, Kalina, & Hendrickson, 1990), each eye projects a single output pathway, the optic nerve, consisting of only about a million axons (Jonas, Schmidt, Muller-Bergh, Schlotzer-Schrehardt, & Naumann, 1992). Between these input and output stages, visual information is transformed across a complex multi-layer neural circuit with not only afferent connections (towards to the brain) but also intra-layer horizontal connections and feedback projections that reach from the upper layers back to the photoreceptors themselves (Masland, 2012).

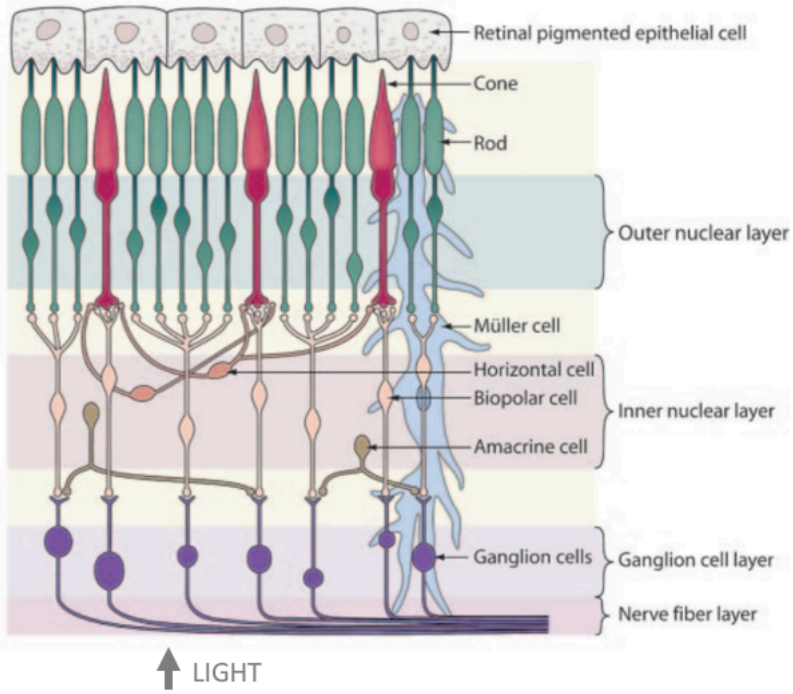



*Figure 7. The neural layers of the vertebrate retina (adapted from Wang et al., 2005). The input layer, the outer nuclear layer, furthest from the incoming light, contains a mosaic of different rod and code photoreceptors. The photoreceptors project to second-order neurons in the inner nuclear layer including the bipolar, horizontal, and amacrine cells. These second order cells in turn project to retinal ganglion cells (RGCs) in the output layer (ganglion cell layer). The RGC axons form the optic nerve, the sole output pathway from the retina.*

The input layer (the outer nuclear layer, furthest from the incoming light), contains the cell bodies for a mosaic of different rod and cone photoreceptors. Cones, that only account for 5% of photoreceptors in the retina (Curcio et al., 1990), predominate in the central region called the fovea. Rods, although far more numerous than cones, particularly in the periphery, are unresponsive at daytime light levels and so photopic vision, that is vision under well-lit conditions, is almost exclusively mediated by cone cells.

As shown in Figure 7, the photoreceptors cells project to second-order neurons in the inner nuclear layer including the bipolar, horizontal, and amacrine cells. These second order cells in turn project to retinal ganglion cells (RGCs) in the output layer (ganglion cell layer). The RGC axons form the optic nerve, the sole output pathway from the retina, and project to central targets including the superior colliculi, suprachiasmatic nuclei, and the lateral geniculate nucleus of the thalamus.

The degree of convergence from photoreceptor, to bipolar cell, to RGC varies with eccentricity and reaches direct throughput (1:1:1) in the most central regions (Curcio & Allen, 1990). In the periphery of retina, in contrast, a single ganglion cell may receive input from hundreds of photoreceptors (Goodchild, Ghosh, & Martin, 1996). Concomitant with lower convergence and a greater density of cone photoreceptors, visual acuity in photopic viewing conditions is highest for foveal vision (Anderson, Mullen, & Hess, 1991; Westheimer, 1965; Weymouth, 1958), corresponding to about 2° visual angle in the visual field, or about the size of thumb held at arm's length (O'Shea, 1991). Acuity drops dramatically from foveal into parafoveal vision that extends 10° around fixation. A movement of just 6° from central vision reduces acuity by 75% (Purves, Augustine, & Fitzpatrick, 2001). Acuity decreases further still moving into the periphery. Thus, for tasks requiring fine spatial resolution, the stimulus must be brought into focus on the fovea. During reading, typical adults make saccadic eye movements at the rate of four or five per second to bring words into foveal vision (Rayner, 1978).

Early electrophysiological recording studies showed that the neural circuits of the vertebrate retina do more than just reduce the resolution of the photoreceptor array before transmitting to central structures. Using excised eyes from freshly pithed bullfrogs (*Rima catesbiana*), Hartline (1938) recorded electrical activity from ganglion as focused points of light were applied to the retina. The individual ganglion only discharged to illumination within a small circumscribed, roughly circular region of the retinal (~1mm) that Hartline termed the "receptive field". Some of the ganglion he recorded from discharged vigorously when lights first turned on within their receptive field and others responded more

vigorously when light was turned off. These different properties were found in closely adjacent cells indicating that ganglion activity does not entirely depend on local conditions of stimulation. Rather, it “appears to be an inherent property of the individual ganglion cells themselves” (Hartline, 1938, p. 401).

In subsequent recording studies in cats, Kuffler (1953) identified a concentric centre-surround organization within receptive fields where mutually antagonistic excitatory 'ON' regions (that increased firing) are surrounded an inhibitory 'OFF' region (that decreased firing) or vice-versa. In an ON receptive field for example, a spot of light confined to the centre region of the receptive field increased cell firing more than a spot of light covering the entire receptive field (Barlow, Fitzhugh, & Kuffler, 1957). Thus, RGCs do not simply register the illumination within a region on the retina, but the *difference* in illumination between a region and its surround. Over the following decade, recording studies identified even more complex feature detectors including direction sensitive RGCs in rabbits (Barlow, Hill, & Levick, 1964) and the now famous ‘fly detector’ ganglion in frogs (Lettvin, Maturana, McCulloch, & Pitts, 1959). In other words, even at the level of the retina, neural circuits are doing more than transmitting point-to-point representations of sensory input; they are extracting spatial features.

By more recent estimates, there are many different types of RGCs, perhaps 15 or more in the human retina, each with distinct physiological properties (Dacey & Gazzaniga, 2004; Field & Chichilnisky, 2007; Masland, 2012). The most well-studied are still the ON and OFF midget and parasol RGCs, accounting for over 70% of ganglia in primate retina (Dacey & Gazzaniga, 2004; Perry, Oehler, & Cowey, 1984; Rodieck & Watanabe, 1993). The midget

ganglia cells are relatively small bodied, have lower conduction rates, and transmit with low temporal but high spatial frequency. Parasol ganglion on the other hand, are relatively large cell bodied, have higher conduction rates, and transmit with high temporal but low spatial frequency. Other cell types, including the intrinsically light sensitive RGCs (Berson, Dunn, & Takao, 2002), are less well understood.

The different RGC types form distinct, parallel sub-circuits (Masland, 2001; Wassle, 2004). For example, the midget and parasol ganglia receive afferents only from M and P sub-types of amacrine and bi-polar cells, respectively. These M and P cells, in turn, have a different profile of photoreceptor projections. Relative to parasol ganglion, midget ganglia receive more cone than rod input and tend to have a lower degree of photoreceptor convergence.

These different RGC sub-circuits form orderly overlapping arrays that precisely tile the retina providing different "views" of the visual field (Gauthier et al., 2009). "It is as if our eye comprises multiple different TV crews pointing their cameras as the same event but each broadcasting to their audience (the relevant brain region) a subjectively cut and processed version of the captured image flow" (Roska & Meister, 2014, p. 163).

In primates, sensory information from the retinae reaches the cortex primarily through the lateral geniculate nucleus (LGN) of the thalamus. An estimated 90% of optic nerve projections terminate in this multi-layered thalamic structure (Perry et al., 1984). Due to a partial decussation of the optic nerve (Figure 8), each LGN receives inputs from the contralateral nasal hemiretina and the ipsilateral temporal hemiretina (Polyak, 1957) thus providing coverage of the contralateral half of the *visual field* (hemifield). Within the LGN

the ipsilateral and contralateral projections terminate on separate layers of the LGN (Polyak, 1957).

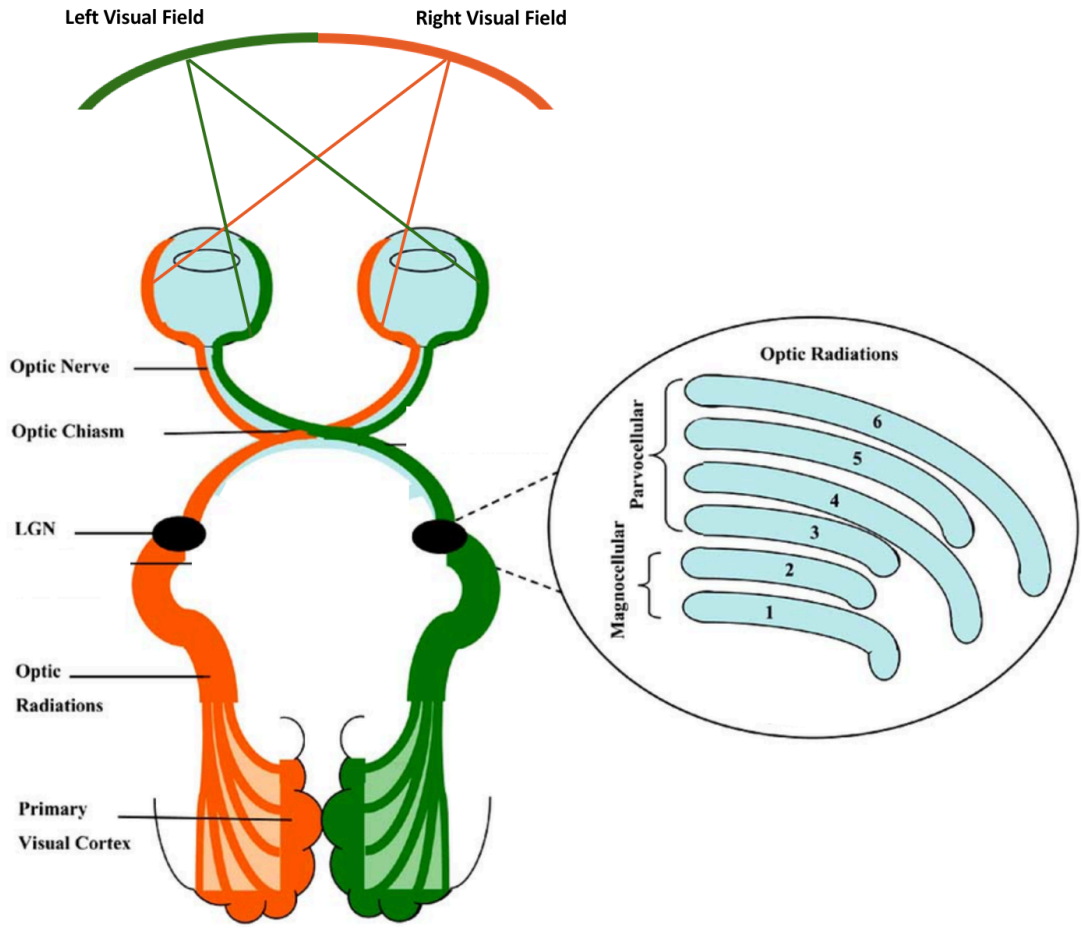



*Figure 8. The projections of the retinogeniculostriate pathway (adapted from Guo, Duggan, & Cordeiro, 2010). Due a partial decussation at the optic chiasm, each retinae project to both the left and right lateral geniculate nucleus (LGN). Projections from the nasal hemiretina are sent to the contralateral LGN and projections from the temporal hemiretina are sent to the ipsilateral LGN. Thus, each LGN receives projections covering the contralateral half of the visual field (hemifield). Within the LGN, retinal projections are segregated to specific laminae according to type. Parasol ganglia predominately terminate on the large bodied cells (magnocellular) of layers 1 and 2 and the midget ganglia predominately terminate on the comparatively small bodied cells (parvocellular) of layers 3-6.*

Projections from different RGC types are also segregated to different lamina of the LGN (Figure 8) with parasol ganglia predominately terminating on the large bodied cells (magnocellular) of layers 1 and 2 and the midget ganglia predominately terminating on the comparatively small bodied cells (parvocellular) of layers 3-6 (Blasdel & Lund, 1983; Livingstone & Hubel, 1987; Nassi & Callaway, 2009; Perry et al., 1984).

Within each layer, the topographic organization of the retina is maintained such that adjacent LGN cells receive projections from adjacent RGCs (Jones, 1985; Reese, 1988). This retinotopic organisation is also in register between layers; for any given cell population in one layer, the cells in the layers directly above or below will encode a similar retinal region (Casagrande & Boyd, 1996).

There are about the same number of LGNs cells as there are RGCs (Van Essen, Newsome, & Maunsell, 1984) and for a long time the LGN was thought to be little more than a simple relay station en route to the striate cortex (Hubel & Wiesel, 1977; Zeki, 1993). This view has been revised on both functional and anatomical grounds. In terms of anatomy, retrograde tracing and other methods have established that retinal afferents account for less than 10% of synapses made on LGN cells (Sherman, 2005; Van Horn, Erisir, & Sherman, 2000). Other sub-cortical systems including the thalamic reticular nucleus and the parabrachial region of brain stem project heavily to the LGN (Van Horn et al., 2000). Among the most numerous source of projections, however, is the striate cortex (Briggs & Usrey, 2009; Casagrande, Sáry, Royal, & Ruiz, 2005; Ichida & Casagrande, 2002). The functional role of this striatal feedback, however, is not well understood. There has long been evidence that antagonistic receptive field surrounds are stronger than those of their retinal inputs (Hubel & Wiesel, 1961). LGN cells also produce fewer spikes than their retinal inputs (Kaplan, Purpura, & Shapley, 1987; Rathbun, Warland, & Usrey, 2010). One hypothesis is that feedback from the striate cortex modulates the relay in dynamic and important ways related to behavioral state, including attention (Sherman, 2005). Perhaps then, the LGN provides a useful final common pathway

where external sources can influence a wide retinotopic range before the massive divergence of projections into the striate cortex.

The roughly 1.5 million LGN neurons project to ~120 million neurons in the primary visual cortex (Van Essen et al., 1984) with nearly half of striatal neurons receiving input deriving from fovea (Wassle, Grunert, Rohrenbeck, & Boycott, 1989). This dense white matter projection, the optic radiation, terminates predominately on layer 4 of the striate cortex. Input from the superior quadrant of the retina, representing the inferior quadrant of the visual field, synapses on the upper bank of the calcarine fissure. Input from the inferior quadrant of the retina, representing the superior quadrant of the visual field, synapses on the lower bank of the calcarine fissure.

The organisation of striatal projections maintains the laminar segregation of the LGN. Magnocellular cells in the LGN terminate predominately on layer 4CB of the striate cortex while parvocellular cells project to layer 4AB (Hubel & Wiesel, 1972; Kaplan, 2013). Ocular dominance columns emerge from multi-layer regions receiving preferential input from one eye or the other (Hubel & Wiesel, 1969). There is an ongoing debate, especially in reading research, about whether the early visual areas receive foveal projections from both or only one hemifield (the bilateral projection theory and split fovea theory respectively; see Ellis & Brysbaert, 2010; Jordan & Paterson, 2010 for recent discussion).

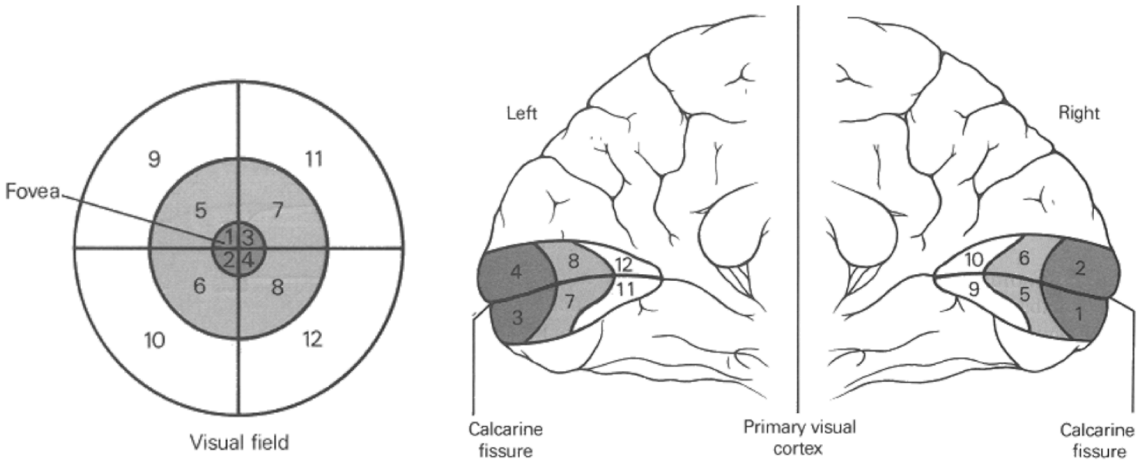



*Figure 9. Visual field representation in the left and right primary visual cortices. In each hemisphere, the superior bank of the calcarine fissure represents the lower quarter of the visual field. The fovea is represented near the occipital pole with representations becoming increasingly more eccentric moving anteriorly (Kandel, Schwartz, & Jessell, 2000)*

Retinotopic organisation (see Figure 9), long known to be a feature of the posterior occipital cortex (Holmes, 1918), is also maintained and the topographic transformation from the retina to the cortical surface has been amply documented both in human (see section 1.7) and non-human primates (Tootell, Switkes, Silverman, & Hamilton, 1988). However, as will be discussed in the next section, receptive fields become more complex in the cortex.

## 1.6. Classical models of visual processing

In this section, I review the first electrophysiological studies of cortical receptive fields (in the striate cortex) and how the evidence from those studies formed the basis of the first hierarchical models of visual processing. I then review how, over the subsequent decades, researchers probed wider and wider regions of primate occipital lobe eventually reaching into the inferior temporal (IT) cortex where remarkably selective receptive fields were found. Accounts of these complex 'object detectors' in the IT, putatively the culmination of converging forward projections and plasticity, inspired many classical hierarchical models of

object processing including, more recently, the LCD model of word recognition (Dehaene et al., 2005).

Using electrodes implanted into the striate cortex of cats, Hubel and Wiesel (1959) were the first to record cortical neurons during visual stimulation and found that cortical receptive fields responded much differently than the receptive fields in the LGN and retina. Of the hundreds of cells sampled, none had the concentric ON/OFF organization characteristic of those early earlier stages of processing. Instead, they were tuned to more complex illumination patterns including line segments of specific orientations (Hubel & Wiesel, 1959, 1962). Like retinal and geniculate neurons, the researchers found distinct excitatory and inhibitory regions within receptive fields of some cells. However, in the case of cortical neurons, these excitatory and inhibitory regions were often organized in an anisotropic rather than concentric arrangement, creating a receptive field tightly tuned to elongated, bar-like patterns of illumination. Within the receptive field, even a 5-10° deviation from the preferred the orientation was usually enough to greatly reduce or abolish the cell's response (Hubel & Wiesel, 1962).

Using short microelectrode penetrations running perpendicular to the cortical surface (i.e. toward the white matter) and longer penetrations running parallel to the surface, the researchers found that receptive fields were organised into orderly columns. For a given point on the cortical surface down to the white matter, neurons in different layers usually had the same orientation preference and coded for a similar region of the retina. Thus, each retina location is represented in the striate cortex many times, first in a column representing

one orientation, then in a column representing another, forming a regular progression through vertical, horizontal, and oblique angles (Hubel & Wiesel, 1962).

In their sample of hundreds of cells in the striate cortex, the researchers distinguished two main cells types that they termed “simple” and “complex” (Hubel & Wiesel, 1962). For simple cells, the stimulus position within the receptive field had to be just right for the cell to fire and even a slight displacement could dramatically decrease firing. Complex cells, on the other hand, were much more tolerant of displacement and fired vigorously to a suitably oriented stimulus almost regardless of where it was in the receptive field. Complex cells also usually had larger receptive fields and lacked identifiable excitatory and inhibitory regions. Further, complex cell, unlike simple cells, were nearly all binocular and could be excited by stimulation to either eye. Importantly, the two cell types were not evenly distributed across the cortical layers. Simple cells were found mainly layer IV, where the majority of LGN projections terminate, and also layer VI. Complex cells were found in layers II, III, and V but never IV.

The simplest explanation for simple and complex receptive fields, Hubel and Wiesel (1962) reasoned, is hierarchy. Complex cells behave as if they receive inputs from many simple cells, all tuned to the same stimuli pattern but coding for slightly different positions on the retina. Simple cells, on the other hand, have identifiable excitatory and inhibitory receptive field regions and behave as if they receive converging projections from ON and OFF LGN cells (see Figure 10). Consistent with this schema, the lowest level of the hierarchy (layer IV) has only simple cells; complex cells, that must be at least a single synaptic stage higher, are never found on this input layer and only populate other (subsequent) lamina.

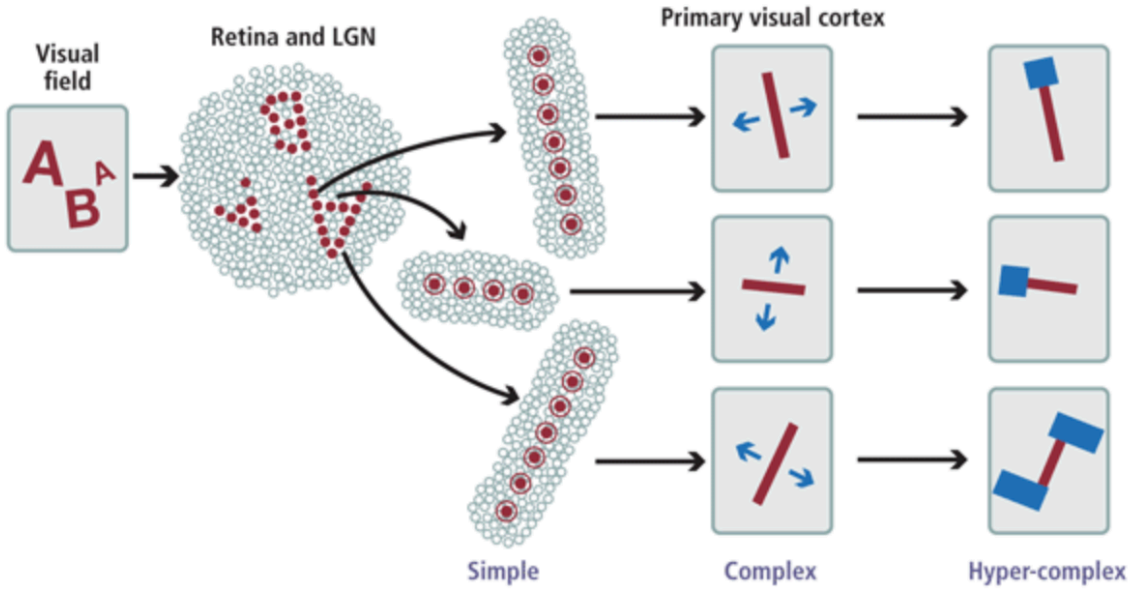



*Figure 10. Cortical receptive fields are more complex than the receptive fields in the retina and LGN. Hubel and Wiesel showed that cells in the striate (1962) and extrastriate cortices (1965) responded most strongly to more complex patterns of light. Unlike the centre-surround receptive fields of retinal and LGN cells, simple cells in the primary visual cortex (striate cortex) had anisotropically arranged excitatory and inhibitory regions and responded most vigorously to elongated, bar-like patterns of illumination (Hubel & Wiesel, 1962). Complex cells also responded to bar-like patterns of illumination but were much more tolerant of displacement and fired vigorously almost regardless of where the bar pattern was in the receptive field (Hubel & Wiesel, 1962). Finally, hyper-complex cells, found only in the extrastriate cortices, had even larger and more complex receptive fields and responded most strongly to a specifically oriented bar of a limited ('stopped') length that did not extend into antagonistic regions (Hubel & Wiesel, 1965). Image adapted from (Wilson, 2010)*

When, several years later, Hubel & Wiesel (1965) first recorded cells in the adjacent prestriate cortex (hereafter "extrastriate" cortex) they found not only complex-like cells, but neurons with even larger and more complex receptive fields that they termed "hyper-complex". Like a complex cell, they responded to bar-like stimuli of specific orientations, however, the length of the stimulus was also important. An optimal stimulus for a hyper-complex cell was a specifically oriented bar of a limited length that did not extend into antagonistic regions. A dozen or so "higher order" hypercomplex cells were also identified that had a similar preference for line-stopped stimuli but responded strongly to two (orthogonal) orientations. The higher-order complex cells also tended to have larger receptive fields than the lower-order hypercomplex order cells (and the lower-order

hypercomplex cells in turn had larger receptive fields than complex cells). Overall, like in the striate cortex, hierarchy and convergence could account for many of receptive field properties found in the sample.

Hubel and Wiesel's (1965) research into extrastriate receptive fields also confirmed that the extrastriate cortex had a second and a third representation of contralateral hemifield field. Moreover, the borders for the three visual areas (I, II, and III) that they defined retinotopically were almost identical to the anatomically defined borders of Brodmann areas (17, 18, and 19) in the cat (Otsuka & Hassler, 1962). Hereafter I will refer to these areas as V1, V2, and V3 respectively.

When Hubel and Wiesel (1965) compared how the simple, complex, and hypercomplex cells were distributed across the three visual areas, they found that complexity tended to increase from V1 to V3. Simple cells, for example, were only found in V1. In V2 there were hypercomplex cells but they only accounted for about 5-10% of the sample, whereas in V3 they accounted for over half. V3 was the only area with higher-order hypercomplex cells. To account for these and earlier findings, Hubel and Wiesel proposed a "tentative" framework where converging projections from lower to higher levels, both within a column and between visual areas, lead to increasingly complex receptive fields (Hubel & Wiesel, 1965). Essentially the same framework is used in the LCD model (Dehaene et al., 2005) where ON/OFF receptive fields in the LGN converge to form oriented bar detectors in V1 that in turn converge to form letter fragment detectors in V2.

In the decade after Hubel and Wiesel's seminal studies, the number of recognised visual areas grew considerably. Electrophyisological recording studies by Allman and Kaas in the owl monkey (Allman & Kaas, 1971a, 1971b, 1974a, 1974b, 1975, 1976) and Zeki in the macaque (Zeki, 1969, 1971, 1977) showed that much of the primate occipital lobe is responsive to visual stimulation. Kaas and colleagues (1971b) recorded from hundreds of sites, canvassing the caudal two-thirds of the owl monkey cortex. Using bar-like patterns of illumination they identified several new visual field maps, even identifying visually responsive areas in the temporal and parietal lobes. One area they found in the middle temporal region had a complete representation of the contralateral half of the visual field (Allman & Kaas, 1971b) and had noticeably heavy myelination that was identifiable even in an unstained brain. The researchers termed this visual area 'MT', for 'middle temporal' area. Soon after there was evidence that MT was specialized for processing motion. In a homologue identified in the macaque (Zeki, 1974), researchers showed that MT, sometimes also referred to as V5 (Shipp & Zeki, 1985), has a high proportion of neurons sensitive to motion (Felleman & Kaas, 1984; Maunsell & Van Essen, 1983; Zeki, 1974, 1978) with receptive fields that are also several times larger than V1 cells (Felleman & Kaas, 1984).

More ventrally, another area called V4 was identified that was also retinotopically organised but instead of motion responsive neurons there were a relatively large proportion of cells selective for specific spectral frequencies (1973). Interestingly, no V4 neurons had receptive fields corresponding to 20° or beyond in the visual field and Zeki (Zeki, 1976; Zeki & Shipp, 1988) proposed that visual areas could be specialized for processing different types of information. After all, such limited coverage of the visual field makes sense for an area specialized for colour; there are almost no cone photoreceptors that far outside the fovea.

Subsequent studies in the macaque also showed that V4 is involved processing shapes and object related forms (Desimone & Schein, 1987; Gallant, Braun, & Van Essen, 1993; Kobatake & Tanaka, 1994).

The most remarkable examples of receptive field selectivity, however, were found in interior temporal (IT) cortex. When Gross and colleagues (1969; 1972) recorded IT cells in anesthetized macaques, they found that receptive fields could be very large and could extend 10° or more beyond the vertical meridian into the ipsilateral hemifield. The receptive fields sampled almost always included representation of the fovea. Like in other visual areas in the macaque, most neurons could be excited by bar-like stimuli, however, some IT neurons could only be excited by much more complex illumination patterns, including cells that strongly preferred outline of hands, especially monkey hands (Gross et al., 1972; see Figure 11). Some cells also showed remarkable position invariance and fired at more or less the same rate regardless of where the preferred stimulus was in its receptive field. Subsequent studies in the macaque also showed that there are small subpopulations of IT neurons tuned to faces (e.g. Desimone, Albright, Gross, & Bruce, 1984; Perrett, Rolls, & Caan, 1982). After only a few training sessions, some IT cells would respond selectively to novel objects that the monkey had just learned to recognize (Logothetis & Pauls, 1995).

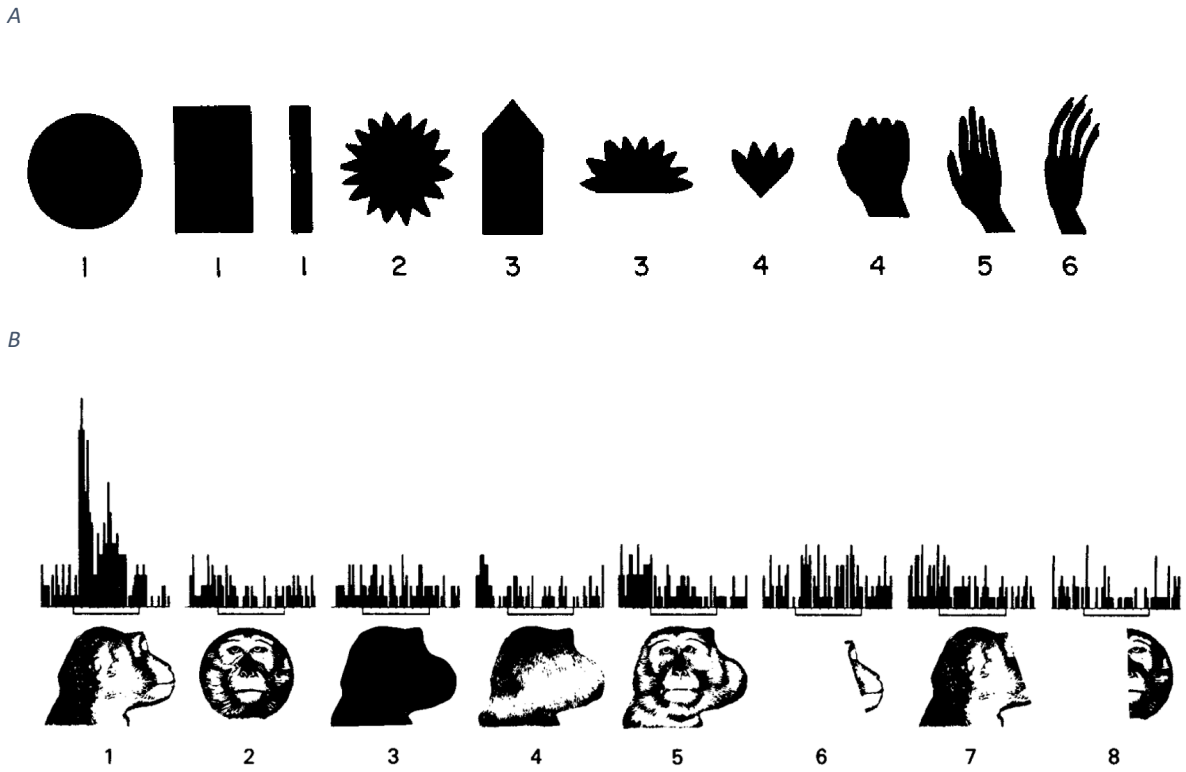



*Figure 11. IT receptive fields can be selective to complex spatial forms. (A) The illumination patterns used to stimulate a group of IT neurons in a monkey (from Gross et al., 1972). The patterns are arranged in order increasing ability to elicit an electrophysiological response from none (1), to little (2-3), to maximum (6). As shown, IT cells were excited by complex illumination patterns, including some populations that strongly preferred outline of hands, especially monkey hands. (B) Activity (spikes/second) of an IT neuron in a monkey during presentation of different face-like stimuli (from Desimone et al., 1984). As shown, changing or removing features of the preferred stimuli (1) eliminated the response.*

As can be seen in Figure 12A, by the early 1980s over a dozen visual areas had been identified in the macaque. Fortunately, a couple of developments brought a degree of order to this ever-growing mosaic of visual areas. The first development took advantage of the differences in how feedback and feedforward projections are distributed across the lamina (e.g. Rockland & Pandya, 1979) to rank and order the visual areas in relation to one another. Using this approach, each area is assigned a specific hierarchical level based on the areas it projects to and the areas it receives projections from (Figure 12B). In these maps, general pathways were identified including, for example, a ventral pathway connecting V1, to V2, to V4, and into IT. Both the LCD model (Dehaene, 2005) and the IA model assume that, during reading, visual information is transmitted along this pathway to the vOT.

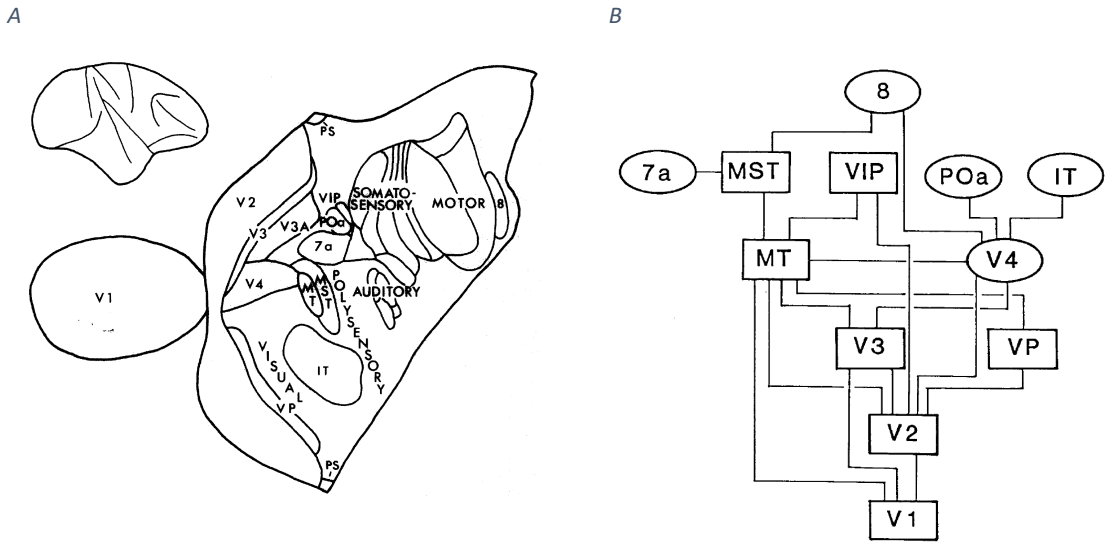



*Figure 12. The identified visual areas in the macaque circa 1980. (A) Visual and non-visual areas are shown on an unfolded map of the right hemisphere (from Van Essen & Maunsell, 1983). (B) The hierarchy of visual areas in the macaque. Each area is assigned to a specific hierarchical level on the basis of its profile of feedforward and feedback connections (Van Essen & Maunsell, 1983). Abbreviations for visual areas: MT (middle temporal), MST (medial superior temporal), VIP (ventral intraparietal), VP (ventral posterior), IT (inferotemporal), POa (Parietal occipital area).*

A second development was related to evidence that entire anatomical pathways are specialized for different functions. In a highly influential paper, Ungerleider and Mishkin (1982) presented neuropsychological, electrophysiological, and behavioural evidence showing that dorsal and ventral pathways are specialised for visuospatial and object form related processing, respectively. For example, monkeys with parietal lesions have severely impaired spatial positioning, but unimpaired object discrimination. In contrast, monkeys with temporal lesions have severely impaired object discrimination, but unimpaired spatial positioning (Pohl, 1973; Ungerleider & Mishkin, 1982).

Neuropsychological evidence also shows that the dorsal and ventral streams likely originate in V1. Monkeys with V1 lesions in regions representing the centre, but not the periphery, of the visual field, are severely impaired on object discrimination (as are monkeys with inferior temporal lesions). Damage to peripheral representations did not impair pattern discrimination performance, however peripheral lesions impaired spatial performance on a landmark task just as strongly as central lesions did. Ungerleider & Mishkin proposed that two different processing streams emerge from V1: (i) a dorsal pathway specialised for visuospatial processing that follows an occipitoparietal route through V1, V2, V3, MT and into parietal and then frontal regions; and (ii) a ventral pathway specialized recognizing objects that follows an occipitotemporal route through V1, V2, V4 and into the temporal lobe. The occipitoparietal and occipitotemporal pathways were thought to derive predominantly from magnocellular and parvocellular inputs respectively (cf. Merigan & Maunsell, 1993) although this division is not clear-cut with ventral areas such as V4 receiving substantial magnocellular input (Ferrera, Nealey, & Maunsell, 1994), and dorsal areas such as MT receiving strong parvocellular input (Nassi, Lyon, & Callaway, 2006).

The LCD model of reading is based on many of these classical principles of primate object recognition including that: (i) the ventral visual stream is specialized for recognizing objects; (ii) the visual cortex is hierarchically organized with converging forward projections creating receptive fields that are increasingly large, complex, and invariant to transformations; (iii) IT neurons are plastic and, through training, can become attuned to any image; and (iv) some visual areas are specialized for processing different visual properties like motion and colour.

The evidence supporting the classical models of object recognition is largely from invasive methods such as intra- and extra-cellular recordings, experimental lesions, and histochemical tract tracing studies. These methods are not available in human studies, except in very rare cases e.g. (Kreiman, Koch, & Fried, 2000; Nobre et al., 1994), and as a result, it is important to consider the extent to which these results parallel findings in humans.

## 1.7. Visual cortex organisation in humans

Prior to 1995, non-invasive neuroimaging methods could not reliably define the borders of visual areas because their size and location vary dramatically across individuals, even when controlling for overall brain volume (Dougherty et al., 2003), and because most border distinctions do not reliably correspond to gross anatomical features (Wandell, Dumoulin, & Brewer, 2007). In 1995, shortly after the blood-oxygen level-dependent (BOLD) contrast was developed for MRI, researchers began combining fMRI with specially designed visual field mapping stimuli to reveal retinotopic organisation in the human occipital cortex (DeYoe et al., 1996; Engel, Glover, & Wandell, 1997; Sereno et al., 1995). Using phase-encoded retinal stimulation, Sereno and colleagues (1995) non-invasively determined the borders of human visual areas V1, V2, V3, and V4. As can be seen in Figure 13, this method reveals a continuous retinotopic organization along polar and eccentricity dimensions. This map provided not only the criteria for accurately defining area borders (i.e. visual field reversal) but also for mapping the retinotopic organization *within* an area, unlike other border drawing approaches like the meridians method (Claeys et al., 2004).

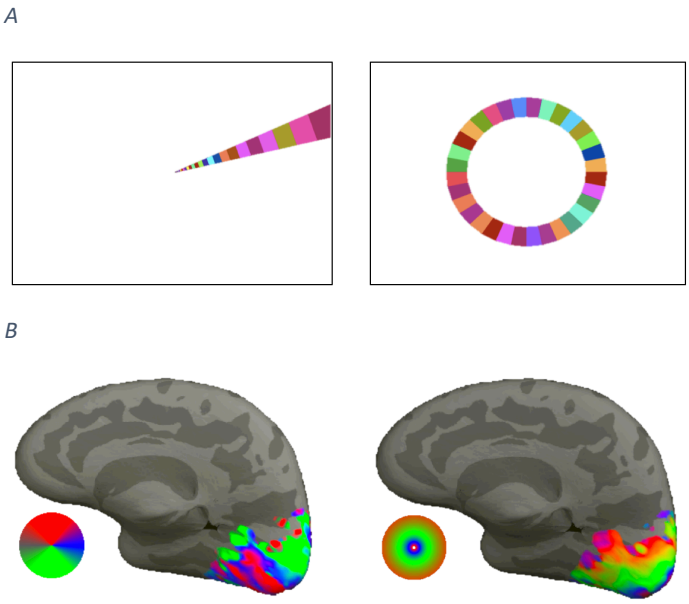



*Figure 13. Phase encoded retinotopic mapping (from Sereno et al., 1995). (A) The polar angle (left) and eccentricity (right) mapping stimuli rotate and expand/contract (respectively) at a constant speed, cycling through the visual field at a regular interval. This cycle frequency is used to calculate the phase of the stimulus (position in the visual field) a voxel's BOLD time series most coherent with. (B) The isoeccentricity and isopolar angle maps shown on a medial view of an inflated right hemisphere. Maps of visual field coverage can be used to accurately and non-invasively define visual area borders (see General Methods for more information)*

Retinotopic mapping techniques using fMRI enabled measurements to be made across the entire visual cortex and are useful when making comparisons between human and non-human primates. Compared to the macaque, visual areas V1, V2 and V3, as well as MT, are conserved in humans but beyond these regions there it is a mixed bag including uncertainty about a human homologue of macaque V4 with some evidence suggesting that ventral and dorsal parts of V4 have evolved differently among primate species (Orban, Van Essen, & Vanduffel, 2004). The monkey IT complex and the human lateral occipital area (LO) complex appear relatively similar (Denys et al., 2004).

Accurate retinotopic maps are important for research into the early stages of reading. First, accurately defining the borders of the early visual areas provides meaningful regions-of-interest (ROIs) that reflect important functional, cytoarchitectural, and connectivity differences in the early visual cortices. Second, retinotopic maps within areas can be used to distinguish neural populations coding for stimulated (e.g. centrally presented visual word) and non-stimulated regions of the visual field. This is useful for distinguishing bottom-up

and top-down influences as predicted by the LCD (Dehaene et al., 2005) and IA (Price & Devlin, 2011) models of reading. For example, according to the LCD model, literacy related changes in the vOT result from an extreme form of perceptual learning (Dehaene et al., 2005) and thus any reading related changes that might be found in early visual cortices should be largely limited to neural populations that most often process the spatial forms of letters and words (i.e. neurons coding for the fovea and parafovea).

## 1.8. Interactive models of visual processing

Neuroimaging and retinotopic mapping techniques provide new insight into how the primate visual cortices are organized and this evidence, along with new data from electophysiological and anatomical methods, led Ungerleider, Mishkin and colleagues to substantially revise their original dual stream framework. The authors argued that the ventral visual pathway much more closely resembles a large recurrent network than a serial, staged hierarchy (Kravitz, Saleem, Baker, Ungerleider, & Mishkin, 2013). In their revised neural framework, areas are connected in much more complicated ways (see Figure 14) with bidirectional connections to adjacent areas as well as reciprocal and non-reciprocal connections to more distant areas that can bypass intermediate regions, enabling direct communication between the formerly early and late stages in the original hierarchy. In this framework, it is difficult to even assign an area to a hierarchy level. Furthermore, how strongly areas are connected to each other varies and by comparing the relative density of projections, the authors identified at least four parallel, yet still somewhat interconnected, occipitotemporal pathways, rather than the single route outlined in earlier proposals. Retinotopic coverage also varies considerably across pathways with systematic differences

in the density of projections relating to contralateral and ipsilateral, upper field and lower field, and central and peripheral input. Importantly, the authors note, this retinotopic bias extends even into anterior inferior temporal regions and this anatomical evidence, along with results from neuroimaging studies showing that high-level visual object representations remain at least somewhat position-dependent, suggest that processing in even the highest levels of the putative hierarchy is not as abstract as previous thought. The differences in retinotopic coverage may even account for why there are clusters of neurons in the occipitotemporal cortex that are (putatively) selective for particular object categories like faces (Downing, Chan, Peelen, Dodds, & Kanwisher, 2006), scenes (Epstein & Kanwisher, 1998), and words (Dehaene & Cohen, 2011). Such clusters, according to the theory, will naturally emerge at cortical locations that afford the necessary retinotopic coverage. This phylogenetic constraint on foveal information might account for why the VWFA is reported to be in such a consistent cortical location across individuals: it develops where there is enough foveal input to support the high-resolution spatial analysis needed for reading.

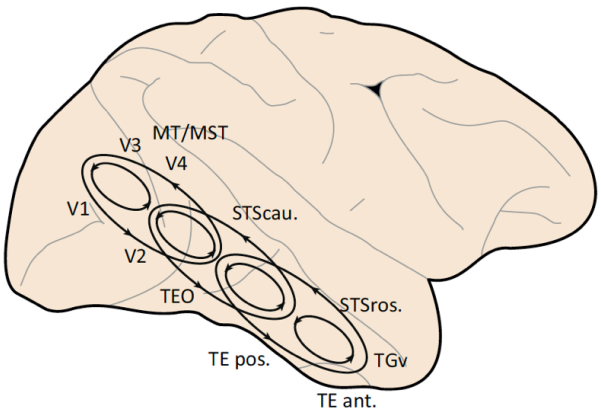



*Figure 14. The revised framework for the ventral visual pathway (from Kravitz et al., 2013). The updated schematic, shown on the lateral right hemisphere surface of the macaque brain, consists of series of overlapping recurrent networks rather than a simple sequence of projections leading from V1 to the anterior IT cortex. Areas have strong bidirectional connections with neighbouring regions as well as longer distance, reciprocal and non-reciprocal connections that bypass intermediate regions. Abbreviations: STS (superior temporal sulcus), TEO (posterior inferior temporal cortex), TE (anterior inferior temporal cortex).*

When one looks closely at the neuroanatomy of the mammalian visual system, there are typically far more top-down than bottom-up projections – a predominance likely extends throughout the primate ventral pathway and early visual areas (Salin & Bullier, 1995). Indeed, only a small proportion V1 inputs convey information from the retina (Budd, 1998; Peters, Payne, & Budd, 1994). Moreover, as Adams and colleagues (Adams, Friston, & Bastos, 2015) point out, V1 neurons receive projections from a far wider area than they project to (Zeki & Shipp, 1988). This loosens the tight retinotopic organisation maintained in the forward projections, enabling feedback to help define the (extra-classical) receptive fields of lower-level cells (Angelucci & Bullier, 2003). In addition to feedback from V2, V1 also receives descending projections from more distal circuits, including some involved in non-visual processing. In monkeys for example, the auditory cortex is directly connected to V1 and sends particularly dense connections to regions representing the periphery of the visual field (Falchier, Clavagnier, Barone, & Kennedy, 2002; Rockland & Ojima, 2003). Evidence from diffusion-weighted tensor imaging (Beer, Plank, & Greenlee, 2011) suggests that there are also auditory-visual projections in humans.

Consistent with a complex bidirectional neural architecture, functional evidence suggests that processing in the early visual areas involves both bottom-up and top-down factors. For example, neuroimaging studies measuring how V1 responds to occlusion (Lee & Nguyen, 2001), visual illusions (Seghier et al., 2000; Stanley & Rubin, 2003) and apparent motion (Muckli, Kohler, Kriegeskorte, & Singer, 2005; Sterzer, Haynes, & Rees, 2006) show that they integrate information from far outside their classically defined visual fields. This integration is likely too far-reaching to be mediated exclusively by the slower-conducting lateral connections (Angelucci & Bullier, 2003) and almost certainly involve top-down feedback

from V2 and beyond. Selectively deactivating V2 feedback, for example, alters V1 receptive fields including their size, surround suppression, and response gain (Nurminen, Merlin, Bijanzadeh, Federer, & Angelucci, 2017). These top-down driven changes to V1 neurons are found despite the monkey being anesthetized, indicating that feedback from V2, and other areas including V5 (Hupé et al., 1998), can be automatically generated and is not dependent on attention.

Spatial attention, on the other hand, shows that top-down activity also depends on the behavioural intentions of the organism. In non-human primates, covertly attending to a location in the visual field influences V1 neurons' coverage of that location, and, similar to the automatically generated influences, also alters receptive field size (Roberts, Delicato, Herrero, Gieselmann, & Thiele, 2007), surround suppression (Sundberg, Mitchell, & Reynolds, 2009), and response gain (McAdams & Maunsell, 1999). In humans, neuroimaging shows that spatial attention elicits an early visual response in corresponding regions of cortex that is nearly as strong as actual visual stimulation (Silver, Ress, & Heeger, 2007). Importantly, this top-down influence also impacts behavior; stronger spatial attention responses correlate with an increased ability to discern the presence or absence of a pattern in the attended region (Ress, Backus, & Heeger, 2000). Thus, early visual processing involves more than just the ascending, retinal signal and integrates modulatory and driving influences from a variety of higher visual systems. Further, consistent with auditory cortex projections into human V1, there is accumulating evidence that auditory signals influence V1 activity (see Petro, Paton, & Muckli, 2017 for a recent review). Even the earliest sensory cortices, it seems, integrate information from disparate systems and modalities.

As expected, given the diverse top-down input in the early visual areas, higher temporal resolution techniques like transcranial magnetic stimulation (TMS) show that the time-course of visual processing in these areas is highly complex and includes dissociable phases of feedforward and feedback activity. In a seminal study, Amassian and colleagues (1989) used TMS to apply millisecond 'virtual lesions' to the posterior occipital lobe as subjects read aloud short strings of visually presented letters. The occipital TMS pulses, that would have disrupted processing in regions of V1 and V2 (Salminen-Vaparanta, Noreika, Revonsuo, Koivisto, & Vanni, 2012; Thielscher, Reichenbach, Ugurbil, & Uludag, 2010), were applied at different times after the stimuli were shown. When TMS was applied 80ms before or 120ms after stimuli presentation, subjects read back nearly all of the letters shown. However, when TMS was applied between 80-120ms, reading performance plummeted. This 'classical dip' in performance has been widely replicated (cf. de Graaf, Koivisto, Jacobs, & Sack, 2014) and likely involves multiple loops of feedforward and feedback activity (Corthout, Hallett, & Cowey, 2003).

TMS studies where two coils are used to apply stimulation to both early visual areas and higher cortical areas (like MT), also show that feedback from higher areas starts having a functional impact around within the classical dip at 90ms after stimulus-onset (e.g. Silvanto, Lavie, & Walsh, 2005). Double-pulse studies using a single coil suggest that there are even later critical periods that may only manifest in more challenging or complex tasks. For example, Juan and Walsh (2003) found that performance on a simple single feature search task was impaired by stimulation during the classical dip, whereas the search of feature conjunctions, a much more challenging task, was also impaired when TMS was applied 200-240ms after stimulus onset.

Spatiotemporal measurements spanning the entire brain show that complex visual tasks like recognising an object or word likely involve integrating information from parallel neural pathways. Using a combination of MEG and fMRI, Bar and colleagues (2006) measured brain activity while subjects performed a visual recognition task on series of familiar objects interposed between two masks. This recognition task is difficult enough that it typically takes subjects several repetitions of the same image before they make a successful identification. The neural response during successful trials, relative to unsuccessful trials for the same image, included a strong orbitofrontal cortex (OFC) response. Crucially, in the left hemisphere this OFC activation peaked 50ms *before* activity peaked in left vOT showing that frontal activity predicts successful recognition *before* activity in the visual cortex. To further investigate the relationship between early visual, OFC, and vOT regions, the researchers analysed how synchronized those regions were on a trial-by-trial basis. Their analysis showed that there was an early phase of coherence (~80ms after stimulus onset) involving the early visual areas and the OFC, that the authors reasoned was consistent with feedforward activity following visual stimulation, and a later phase (~130ms after stimulus onset) involving the OFC and vOT that they suggest was likely due to feedback activity. Moreover, successfully recognizing a picture was associated with longer late-phase synchrony, and, interestingly, when the researchers made recognizing objects much easier by un-masking the objects (and presenting them for longer durations), the OFC response all but disappeared indicating that frontal structures may only be recruited for more difficult tasks.

The nature of the information being sent so quickly to OFC, however, was unclear. Following an earlier hypothesis (Bar, 2003), the researchers proposed that that low spatial frequency representations images are sent to the OFC, possibly through the dorsal magnocellular pathway, and this low resolution representation is used to aid recognition in other cortical structures. To test the theory, the researchers, measured brain activity in separate fMRI and MEG scanning sessions while subjects viewed two sets of filtered stimuli: (i) predominantly low spatial frequency images; and (ii) predominantly high spatial frequencies images. In line with predictions, BOLD signal change and MEG current amplitudes both showed that the OFC responded much more strongly to low spatial frequency than to high spatial frequencies images. The researchers proposed that the OFC uses low spatial frequency representations to make an 'initial guess' that it then feeds back to the temporal cortex in way that sensitizes that object representation and aids recognition performance. In cases when objects are easy to recognise, like in the unmasked condition they tested, recognition is so rapid and efficient that there is very little demand for top-down facilitation (Bar et al., 2006).

During reading, frontal circuits also respond very quickly. Event-related MEG measurements show that about 100ms after words are shown, the inferior frontal gyrus (IFG) is active and responding in phase with VOT circuits (Pammer et al., 2004). Moreover, in this early phase (~100-300ms), the frontal region responds even more quickly to anagrams of words (HUOSE) than to the words themselves (HOUSE). In contrast, left vOT responds significantly more slowly to the anagrams than words. Thus, similar to the results of Bar and colleagues (2006), frontal activity does, in some recognition tasks and for some stimuli conditions at least, precede activity in vOT. The frontal region that responded early in Pammer et al.

(2004) corresponds to posterior aspect Broca's area in the inferior frontal gyrus (IFG), a region widely regarded to play are role in phonological and articulatory processes. The researchers proposed that the IFG is involved in early phonological processing that is then fed back to facilitate grapheme–phoneme mapping in vOT. Consistent with this proposal, recent dynamic causal modelling of MEG data does suggest that the IFG does sends information back to left vOT during reading (Woodhead et al., 2014). Further, recent MEG evidence also shows that during reading, the early IFG response is sensitive to phonological priming (Wheat, Cornelissen, Frost, & Hansen, 2010). Wheat et al (2010) argued that their results, when considered along with evidence showing that the IPL and middle occipital gyrus were anatomically (Wakana et al., 2004; Bernal and Altman, 2010) and functionally (Kujala et al., 2007) connected, suggest that information is sent from occipital visual areas to the IFG along a fast route (superior longitudinal fasciculus) that bypasses vOT. This raises the possibility that the ventral route (V1, V2, V4, vOT) may not be the only pathway involved in early word recognition.

## 1.9. Reading research into early visual processing

Over the last few decades, most of the research into the initial visual stages of reading have targeted occipitotemporal structures and there has been surprisingly little effort aimed at investigating how the early visual cortices are involved. In fact, reading investigations commonly use methods that all but factor out activity in these early areas. As some of the first neuroimaging studies showed (Petersen, Fox, Snyder, & Raichle, 1990; Wise, Hadar, Howard, & Patterson, 1991), the contrast between false fonts, consonant strings, and word stimuli subtracts away nearly all of the bilateral occipital activation found when those

individual conditions are compared to fixation or rest. Effectively investigating how these areas respond during reading requires methods better tailored to the properties of the early visual system.

In the parallel recurrent network of the primate visual system, *where* neural activation is detected is not necessarily a reliable indicator of *when* that region is involved in a particular process – especially in the case of fMRI or PET measurements where neural activity is pooled over several seconds. Using MEG's greater temporal resolution, Tarkiainen and colleagues (1999) measured neural responses to visually presented single letters, two-letter syllables, four letter words, and symbol strings of equal length (i.e. one, two, and four character symbol strings). Using a factorial design, each stimuli type was also crossed with four levels of visual noise. The earliest stimuli effect they found, involving greater activation for both higher levels of noise and longer strings, occurred about 100ms after stimulus onset and originated in the bilateral area surrounding V1 and extending ventrolaterally as far as V4. There was however, no main effect of stimulus type indicating that at that stage, symbols and letters were being processed in a similar way. Approximately 50ms later, a second dissociation was found that was left-lateralised and located in the ventral occipitotemporal region (vOT). This later response included greater activation for letter strings, especially words. Unlike the earlier effect, the response was diminished at the highest noise level. This later response, it seemed, was more sensitive to the content of stimuli; when not obscured by noise, vOT responded more strongly to letters and words than to symbol strings of the same length. The authors suggested that the early response, that they called 'Type-I' activity, resulted from basic visual processing common to all the visual stimuli with areas V1-V4v being more sensitive to the low-level differences introduced

by noise, including, for example, the addition of luminance contrast borders. This is consistent with previous fMRI studies that found that noisy, scrambled stimuli elicit stronger responses in early visual cortices that non-scrambled stimuli (Allison et al., 1994; Grill-Spector, Kushnir, Edelman, Itzchak, & Malach, 1998; Malach et al., 1995). The later 'Type-II' activity, the researchers argued, suggests that left vOT is sensitive to written language forms (letter and word strings), presumably developed through extensive exposure to writing, and may provide a cortical interface between visual and linguistic representations. The researchers, however, stopped short of proposing that this region was a dedicated visual word form system, partly because when two of their participants were shown unfamiliar rotated-letter stimuli, their left vOT response was just as strong as it was for regular letter string stimuli, making it less likely that the region has an entirely experience-derived specialisation for writing. Nonetheless, this research provides compelling spatiotemporal evidence that circuits in left vOT play an early role in processing word stimuli.

Importantly, comparisons using letter-strings and symbols are confounded by differences in visual complexity, familiarity, and other attributes; when uncontrolled, these differences may affect how brain regions respond the stimuli. To work around this, researchers have used properties of alphabetic writing systems to control some of these differences. Using English, Woolams and colleagues (2011) designed a set of letter string stimuli that had an identical number of letters and syllables but differed in terms of (i) whether they were a word or not and (ii) whether their component bigrams were frequent or infrequent. Using fMRI, the researchers measured brain activity while subjects performed a visual lexical decisions task on these stimuli and found a lexicality effect in left vOT, replicating the previous finding of greater activation for pseudowords than words in the region

(Kronbichler et al., 2007). They also found a frequency effect with higher activation found for infrequent than frequent strings, irrespective of whether the string formed a word or not, in a cortical region 30mm *posterior* to left vOT, where the lexicality effect was found. Importantly, because this experiment used only letter strings and not symbols or false fonts, it is difficult to attribute the effects to low-level differences between the stimuli conditions. After all, the strings are all built from the same small set of familiar characters (i.e. the English alphabet). Instead, the authors suggested that the posterior left occipitotemporal region responds more strongly to infrequent than frequent letter combinations because it is sensitive to how often sub-lexical combinations are encountered in writing. Interestingly, Vinckier et al. (2007) also found sub-lexical effects in the region but in contrast to the Woollams et al (2011) study, infrequent combinations elicited a *smaller* response than frequent combinations. This difference, Woollams et al. (2011) reasoned, was likely due to the different tasks used in the two studies. Subjects in the Woollams et al. (2011) study made lexical decisions and in the Vinckier et al. (2007) experiment, subjects performed an odd-ball detection task.

Tasks differences, even when identical stimuli are used, affect activity in regions of the ventral visual pathway including left vOT (Mano et al., 2013; Yang & Zevin, 2014). For example, Yang and Zevin (2014) used fMRI to measure brain activity while subjects performed a lexical decision task and a symbol detection task on the same set of stimuli. Like the stimuli used in the Vinckier et al. (2007) study, there was a hierarchy of word-likeness with conditions ranging from false-font strings, letter strings with infrequent bigrams, letter strings with frequent bigrams, pseudowords, and finally word strings. Despite the exact same stimuli being used in both the lexical decisions and symbol detection

tasks, there was a main effect of task with left vOT responding more strongly during lexical decisions. The results suggest that during reading, higher-level task demands influence occipital-temporal processing.

Results from outside the reading literature suggest that top-down influences affect processing in even earlier regions reaching all the way back to the posterior occipital areas (see Gilbert & Li, 2013 for a recent review). Indeed, in experiments that accurately map the borders of the early visual areas, even V1's response to simple visual stimuli (e.g. moving dots) has been found to depend on the behavioural intentions of the subjects (Huk & Heeger, 2000; Watanabe et al., 1998). Such task-dependent processing represents a challenge when investigating the initial stages of reading and limits the conclusions that can be drawn from studies using a single task.

Another limitation is that reading investigations rarely map the borders of visual areas and this lack of definition obscures comparisons between studies. For example, it is difficult to tell which 'pre-VOT' area the Woollams et al. (2011) and Vinckier et al. (2007) results point to. Quite a bit is known about the properties of the different early visual areas, especially where there is homology with non-human primates, and accurate area maps would allow reading results to be related back to that evidence. Futhermore, the early visual areas have distinct topographic, cytoarchitecural, connectivity, and functional properties so mapping these areas as distinct regions of interest increases the sensitivity of investigations involving the early visual areas.

To date, only a handful of reading experiments have mapped early visual areas as specific regions-of-interest. Szwed and colleagues (2011), using fMRI and a meridian mapping method (Claeys et al., 2004), functionally defined the borders of V1/V2 and V3v/V4 in each of their subjects. The subjects were then scanned while passively viewing (i) French words and (ii) scrambled words that were meticulously designed to match un-scrambled stimuli on line length, luminance, and number of vertices – that is, low level visual properties. Even with these controls, bilateral V1/V2 and V3v/V4 responded stronger to intact than scrambled words. To help rule out that this word advantage could still be due to some unforeseen and uncontrolled low-level visual differences between two stimuli conditions, Szwed and colleagues (2014) conducted a follow-up study where they held stimuli factors constant and instead varied the reading expertise of their subjects by comparing groups of French and Chinese monolinguals. Once again V1/V2 responded more strongly to the French words than to the scrambled French words, but crucially only in French readers (and this time only in left hemisphere). For Chinese subjects, V1/V2 responded just as strongly to both conditions (in both scripts). In left V3/V4 however, Chinese words elicited a stronger response than the scrambled Chinese words or the French stimuli. This word advantage was not seen in the right hemisphere. Since the stimuli and task requirements were exactly the same between the groups, the authors argued that the differences in V1/V2 (French subjects) and V3/V4 (Chinese subjects) must result from differences in reading expertise and that extensive exposure to a writing system, perhaps through a mechanism similar to perceptual learning (McManus, Li, & Gilbert, 2011; Sigman et al., 2005), leads to a degree of specialisation for spatial forms of that writing system. Although the meridians mapping method does not map retinotopy *within* an area, the researchers estimated that responses were strongest in central representations near horizontal meridian. This is consistent

perceptual learning and LCD model predictions as the reading effects were strongest where words are most frequently seen.

Dehaene and colleagues (Dehaene et al., 2010) used a similar approach and functionally defined areas V1/V2 in groups of literates, illiterates, and ex-literates (acquired literacy in adulthood) subjects. Using fMRI and an oddball detection task they measured how V1/V2 responded to a range of visually presented stimuli including letters, false fonts, tools, faces, moving checkerboards, and pictures. When they analysed the brain activity they found that, across stimuli conditions, bilateral occipital activity was stronger in literates. Moreover, literacy was also associated with a stronger activity in a bilateral region in V1 with a preference for horizontal checkerboards. This bilateral region responded much more strongly to horizontal than vertical checkerboards and this advantage was significantly greater in the left than right hemisphere. Further, reading ability was a factor in how strongly this region responded to horizontal (but not vertical) checkerboards. Literate brains respond more strongly to horizontal orientated checker boards, the researchers suggested, because of perceptual learning and the literates' extensive exposure to words presented along the horizontal meridian of the visual field, where words appear under typical, everyday reading conditions. Again, with the limits of the meridians method used, it was unclear if this putative perceptual learning effect aligned with the expected retinotopic extent of the stimuli (and typical reading conditions more generally) as would be predicted if this effect was due to reading experience.

Several years later, the researchers repeated the same experiment with a similar sample of literate, illiterate, and ex-literate subjects, but instead of using fMRI they used EEG and

analyzed event-related potentials (Pegado et al., 2014). To their surprise, they found that the P1 window (∼100 ms), that is thought to reflect striate and extrastriate activity, was unaffected by literacy. A literacy-effect, however, was found in the posterior occipital voltages later on, just after N1 (~200-240ms), with better readers responding more strongly across stimuli types. If literacy effects take hold later, as the ERP data suggests, then the V1/V2 literacy-influenced activity found in the previous fMRI study (Dehaene et al., 2010) likely results from subsequent top-down activity in those areas pooling together in the BOLD signal change.

It also may be the case that top-down influences on early visual processing are easier to detect during more demanding or realistic reading conditions. For example, in an MEG study of sentential reading, Dikker and colleagues (2009) found that their syntactic category manipulations affected processing surprisingly early (M100 response), likely in areas V1/V2. This result was particularly striking as the M100 response has been extensively studied using words in isolation and had previously (Tarkiainen et al., 1999) only shown sensitivity to variation in stimulus noise and length and not linguistic variables.

Although difficult to relate to specific neuroanatomical structures, behavioural studies have nonetheless greatly informed our thinking about the early stages of reading including the potentially important role feedback plays in recognising letters and words. A classic example is the faciliatory effect word context has on letter perception, known as the word superiority effect (Cattell, 1886; Reicher, 1969; Wheeler, 1970). Cattell (1886) demonstrated that for very brief exposures, participants were better at recalling letters when they were embedded in words than when they were embedded in equally long strings

of unrelated letters. This faciliatory effect is seemingly at odds with a strictly bottom-up account of word recognition. Rather, the results suggest that word-level information influences the perception of the letters they are comprised of. One possible alternative explanation, however, was that the words were just easier to hold in memory than non-words and thus participants were better able to recall individual letters. Similarly, the greater familiarity of words could be used to to make more informed guesses of target letters. To test these possible explanations, Reicher (1969) developed an innovative method involving stimulus masking and a forced-choice paradigm. In the experiment, participants were shown a target stimulus (e.g. WORD) that was almost immediately followed by a mask (#####). The participants were then forced to make a choice between two letter options (e.g. D and K). Crucially, both letter alternatives formed equally likely words (e.g., WORD and WORK) so guessing on the basis of partial information (e.g., WOR?) was no better than chance. Further, since the task only demanded a choice between two single letters, memory load was unlikely to be a major factor in performance. To investigate a potential word superiority effect, two other conditions were included: non-word anagrams of the same words (ORWD) and the target letters presented in isolation (D, K). Overall, participants were more accurate at recalling letters when they were embedded in words than when they were embedded in non-word anagrams or presented in isolation. This result, replicated a year later by Wheeler (1970), suggested that Cattell's word advantage did reflect something meaningful in how we process words. Today, the Word Superiority Effect (WSE), or the Reicher-Wheeler Effect as the phenomenon is also known, is considered strong evidence that letter perception and word recognition cannot be strictly bottom-up and must be at least somewhat bidirectional.

Indeed, by allowing activity on the word-level to influence processing on the letter level, computational models can successfully replicate the WSE. In a seminal paper, McClelland and Rummelhart (1981) introduced an innovative bidirectional model of word perception, the Interactive Activation model (IAM), and described how it performed during computer simulations where a range of inputs were tested including a set of masked letter strings designed to be consistent with the stimuli used in Reicher's (1969) force-choice paradigm. The IAM has three representational layers: visual features, letters, and words that interact via feed-forward and feed-back connections. Following input (e.g. WORD), activation increases in the corresponding visual features. Those visual features in turn activate (via excitatory connections) all the letter detectors that share that visual feature while at the same time deactivating (via inhibitory connections) those that do not. As the letter activations grow stronger, they in turn activate the word detectors containing those letters (in the corresponding position) and inhibiting those that do not. On the word level, word detectors mutually inhibit each other through lateral inhibitory connections, and, crucially, also send connections (both inhibitory and excitatory) back down to the letter nodes enabling word representations to interact with on-going letter-level processing.

When the IAM was tested in computer simulations using the Reicher-inspired input strings, letters were found to be more perceptible when they were embedded in words than when they were embedded in consonant strings or presented in isolation. Furthermore, letters were more perceptible when presented in orthographically valid pseudowords, replicating a 'pseudo-word superiority effect' also found when humans read (Baron & Thurston, 1973; Spoehr & Smith, 1975). Overall, the IAM results showed remarkably similar effect sizes to several important behavioural studies including the original Reicher-Wheeler

experiments and today, feedback and interactivity are practically ubiquitous features in computational models of reading (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; Harm & Seidenberg, 2004; Jacobs, Graf, & Kinder, 2003; Perry, Ziegler, & Zorzi, 2007; Plaut, McClelland, Seidenberg, & Patterson, 1996; although see Norris, McQueen, & Cutler, 2000 and Paap, Newsome, McDonald, & Schvaneveldt, 1982 for feedforward accounts of the WSE).

Given how central the principle of interaction is to both cognitive and computational models of visual word recognition, it is perhaps surprising that the classic neurological model of reading (Dejerine, 1891) and a more recent instantiation (Dehaene et al., 2005) eschew feedback connections and focus entirely on feedforward explanations (Cohen et al., 2002; Dehaene et al., 2005; Kronbichler et al., 2004). This may be due in part to the fact that the prototypical evidence for interactivity, the word superiority effect, is purely behavioural – there is no corresponding effect in the functional imaging literature. There are, however, biological signatures of interaction in vOT during reading. For instance, if vOT is the site of pre-lexical bigram detectors, how can one explain lexical frequency effects (e.g. Kronbichler et al., 2004) or pseudohomophone effects (Twomey et al., 2011) without feedback from higher order representations? Similarly, why does the region show repetition priming for words but not pseudowords (Devlin, Jamison, Gonnerman, & Matthews, 2006; Fiebach, Gruber, & Supp, 2005) and cross-modal priming for word-picture pairs (Kherif et al., 2011)? Each of these effects has a straightforward explanation when considered in a predictive coding framework where top-down predictions are matched to bottom-up inputs (Price & Devlin, 2011) but are challenging to explain in a purely feed-forward framework. It is noteworthy that to date, feedforward proponents have not offered any explanations for

these effects. Dehaene and Cohen (2011) acknowledge that explicit attention can drive top-down effects that "optionally recruit" vOT such as when participants are verbally asked to imagine writing text (Cohen et al., 2002; see also Dehaene, 2010) but otherwise explicitly deny the role of automatic top-down contributions to visual word recognition.

## 1.10. Testing hypothesis

The key question regarding the neurobiology of reading, at least in terms of the early stages of word recognition, is whether sensory-encoded words must first be recoded into abstract orthographic forms (in left vOT) before linking with linguistic representations or if reading is more interactive with top-down input from language and other related circuits influencing processing earlier on. These two views make contrasting and testable predictions about how the early visual areas respond during reading. Among the most conclusive evidence would be data showing that higher-order linguistic information influences processing before the putative orthographic encoding stage. For example, some have argued that the word frequency effects in the left vOT are evidence for whole-word neural detectors (Kronbichler et al., 2004). A word frequency effect in V1-V3, where the notion of whole-word detectors is absurd, would be strong evidence against this interpretation.

Testing these contrasting views requires methods tailored to the properties of the early visual system. The emerging view of this system is that, from the retina onwards, activity is highly bidirectional and, in the cortex, visual areas receive reciprocal and non-reciprocal projections from a wide range of cortico-cortico and subcortical structures. Importantly, different areas have different connectivity, cytoarchitecural, and functional properties. A

limitation of previous investigations into the early visual contributions of reading is the lack of accurate retinotopic maps of early visual areas. Accurate borders and retinotopic maps are important to the current investigations for two main reasons. First, neuroanatomical studies have shown that these early visual areas differ considerably in terms of how they are connected to other cortical and sub-cortical circuits. A central prediction of interactive account is that the activity of early visual areas during reading will be a product of not only of the processing of the ascending sensory signal but of the top-down influences that depend on the specific profile of afferents into that area. Second, reading is a heavily fovea-dependent task and a prediction of the LCD model is that if there are any sensitivities to words or letters posterior to the vOT, that sensitivity will be greatest in regions within V1, V2, and V3 that code the central region of the visual field along the horizontal meridian where words appear during fixation.

Chapter 2 describes the key methods used in this thesis, including how accurate retinotopic maps can be non-invasively acquired in human subjects. I also describe how the reading stimuli and tasks were designed in order to maximise sensitivity to top-down influences while minimizing a wide range of potential confounds. Three main methodological steps were taken to help distinguish a top-down signal, that is likely to be subtler and more modulatory, from the driving activity of the ascending sensory processing. First, a set of letter string stimuli were designed that allowed a word-level property, lexical frequency, to be manipulated while also tightly controlling for lower-level differences including bigram and trigram frequency that have been previously shown to influence processing in early occipitotemporal regions (Woollams et al., 2011; Hauk et al., 2008; Kronbichler et al., 2004). Second, each subject performed five different reading tasks that all used the same stimuli

set but that emphasized different aspects of reading. Finally, an atypically large number of stimuli trials were acquired for each task to maximize sensitivity. In addition, all analyses were conducted in subject-specific space in order to maintain precise links between retinotopically defined regions and the patterns of activation due to reading.

Chapter 3 investigates whether there is evidence of top-down modulation of early visual areas (i.e V1-V3) in addition to the bottom-up activity that one expects. In order to compare the results to previous studies, vOT is included in all of the analyses. These focus primarily on task- and stimuli-effects. In particular, if a high-level attribute like lexical frequency can affect activation in areas V1, V2, and V3 then this would provide strong evidence for top-down modulation and interactivity.

Chapter 4 extends the investigation into higher order visual areas and further investigates whether reading-related activation is primarily present in ventral stream regions (V4, VO-1, VO-2) or is also present in dorsal stream areas (V3a, V3b, V7). In addition, it investigates the contribution from MT, a region sometimes implicated in reading disorders such as dyslexia (Stein & Walsh, 1997).

Chapter 5 reports a surprising finding, namely that one of the five reading tasks produced a very different pattern of activation than the other four. The chapter investigates whether this is a genuine task effect or is the consequence of low-level differences in the paradigm such as the timing parameters of the stimulus presentation.

Chapter 6 develops some general conclusions from the experimental work presented in this thesis, reviewing its main contributions, their implications and their limitations.

# *2. General Methods*

My investigations into how the early retinotopic cortices contribute to reading required overcoming three main methodological challenges. First, for each participant, I needed to accurately map the borders and retinotopy of several areas of interest (V1, V2, V3, V3A/B, hV4, V5/MT, and V7) so that I could assess their distinct contributions to reading. Second, I needed to develop a set of experimental reading tasks that could probe different aspects of reading in order to explore a range of potential contributions within these areas. Third and finally, the reading tasks and stimuli needed to be designed in a way that allowed higher-level linguistic properties to be manipulated while at the same time controlling for low-level visual differences that the early visual cortices will be particularly sensitive to.

Further, to maintain the accuracy of the visual ROIs and the sensitivity of the subsequent reading investigations, all neural response data needed to be analysed in participant space rather than registering to a group or standard space that would inevitably reduce fidelity through averaging. I also opted for a multi-case study approach (n=4) so that I could investigate how the visual ROIs respond to a wide range of reading task and stimuli manipulations. I acquired approximately 4 hours of scanning data per participant.

## 2.1. Participants

The same four participants participated in all three experiments (3 male, aged 35, 36, and 42; 1 female, aged 30). The participants were monolingual native English speakers with normal or corrected-to-normal vision and no history of reading or neurological disorder. They provided informed consent following an overview of the experimental procedure. The experiment was approved by the UCL Research Ethics Committee (fMRI/2008/010).

A multi-case approach was well-suited for the present experiments for a number of reasons relating to the properties of the early visual cortices. First, visual areas defined using retinotopic criteria provide meaningful regions-of-interest (ROIs) that reflect important functional, cytoarchitectural, and connectivity differences and this allows neural responses during reading to be investigated using more sensitive ROI-based analyses rather than whole-brain comparisons. The method used to acquire the retinotopy information used here required approximately 75 minutes of data collection per participant, as well as subsequent manual delineation of each ROI. This is a time-consuming process, but essential given my research question. Second, the visual field maps of visual areas V1-V3 are particularly well-defined, allowing me to distinguish between 'stimulated' and 'non-stimulated' cortical populations coding for, respectively, the central location in the visual field where the stimulus appeared and the more peripheral regions of the visual field lying beyond the visuotopic extent of the stimuli. This distinction also opens the possibility of distinguishing between the ascending retinotopically-bound visual signal and potentially more spatially diffuse, top-down modulation. Third, there is evidence, from several different experimental paradigms using fMRI, that top-down influences on early visual areas V1-V3 can elicit very large and detectable increases in BOLD response. For example, the allocation of spatial attention to a non-stimulated region of the visual field can elicit a BOLD response that is similar in magnitude to actual appearance of a stimulus in that location (Silver et al., 2007).

## 2.2. Visual areas were mapped using phase-encoded retinotopic mapping

Non-invasive mapping of visual field coverage in humans was first demonstrated in the mid 1990s (DeYoe et al., 1996; Engel et al., 1997; Sereno et al., 1995). This phase-encoded retinotopic mapping technique has since been applied in numerous other labs (Dumoulin et al., 2003; Wandell, Brewer, & Dougherty, 2005; Warnking et al., 2002) and is now the preferred approach for in vivo delineation of early visual areal borders in human subjects. This method (Sereno et al., 1995) was used here to accurately map the borders and retinotopy of the visual ROIs in each of the four participants. The borders of the visual ROIs were defined before the reading data were acquired so as not to bias the results.

Phase-encoded retinotopic mapping techniques work by combining neuroimaging with specially designed visual mapping stimuli that traverse the visual field at regular intervals. Mapping typically involves two stimuli types: a wedge that rotates 360° through the visual field and an expanding/contracting annulus (see Figure 15). These stimuli elicit a periodic rising and falling pattern of activation as the stimulus enters and exits the receptive fields of neurons, hence the name 'travelling wave' retinotopic mapping. Figure 15 illustrates this process for two different visually responsive neural populations (e.g. voxels), shown as a red and a green circle. Because the moving wedge begins in a vertical orientation, the red circle is strongly stimulated immediately and this quickly decreases as the phase of the wedge increases (i.e. it begins to rotate away from this region). As the wedge completes the circle, activation in the red circle increases again, producing a cosine-wave with a frequency matching the frequency that the stimuli cycles through the visual field. In contrast, the green circle is not initially stimulated and only increases activity as the wedge approaches

90°. Its response is a sine-wave with that frequency – or in other words, it responds with the same frequency as the red circle but out of phase by 90° ($\pi$/2 radians). Because the wave frequency is known (i.e. the frequency of the stimulus cycle), all that is needed to map a voxel to its preferred stimulus location is to determine the phase of the frequency that the voxel is most coherent with. This can be done using a Fourier transform. By analyzing at least two sets of stimuli runs, one that presents all polar angles at the given frequency per scan (e.g. the rotating wedge stimuli), and other that presents all eccentricities at a given frequency per scan (e.g. the expanding/contracting annulus), a voxel's preferred (most coherent) X and Y coordinates in the visual field can be estimated. These data are often displayed individually as isoeccentricity and isopolar-angle color coded maps overlaid on anatomical data. Typically, there are around 6-8 stimulus cycles per scan in order to acquire enough undulating activation in the time series data for the mapping analysis.

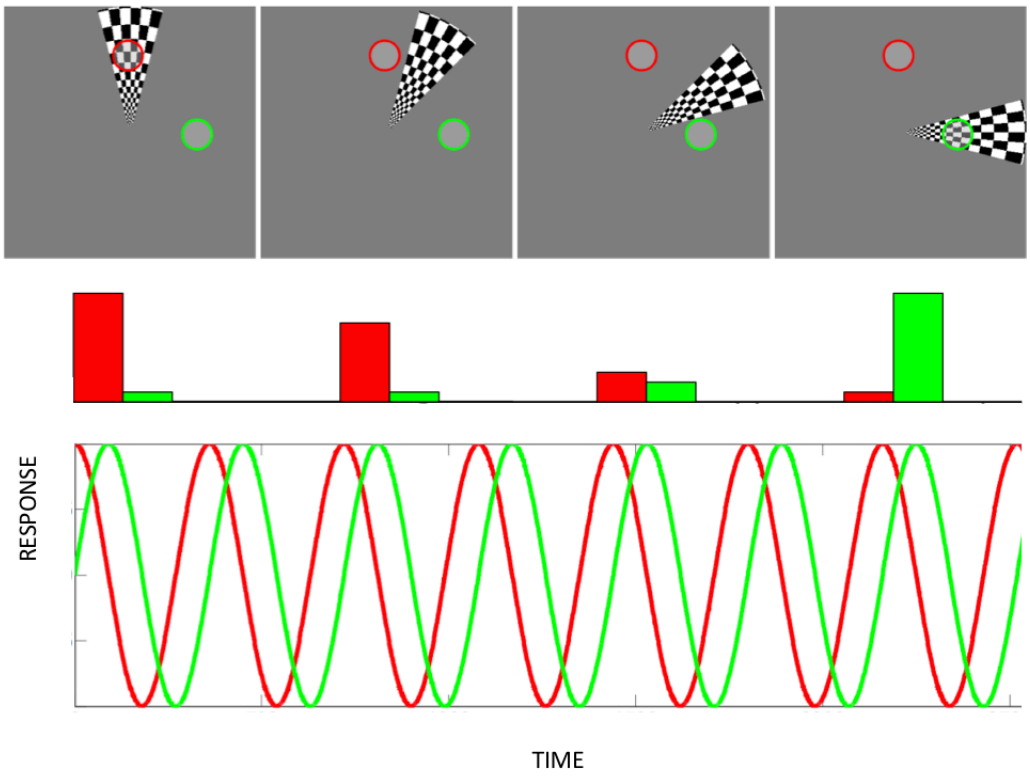



*Figure 15. Phase-encoded retinotopic mapping (adapted from Schwarzkopf, 2010). (Top) A wedge stimulus, used to map polar angle representation, rotates around a central point and cycles 360° through the visual field at a regular frequency. As the stimulus passes out of the receptive fields of one population of neurons (red circle) and into another (green) it elicits an undulating wave of rising and falling activation. (Middle) neural activity (e.g. BOLD signal) is high in the red population when the stimulus is at a vertical orientation and decreases as the stimulus progresses to a horizontal orientation (90°). In contrast, activity in green population is weak when the stimulus in in the vertical position and only increases activity as the wedge approaches 90°. (Bottom) Idealized neural response of the red and green neural populations. The response of both populations is a sine-wave with the same frequency as a stimuli cycle but a different phase. For a population of neurons (e.g. voxel), the most coherent phase (and thus position of the stimuli in the visual field) can be found using a Fourier transform. When combined with the results of eccentricity mapping, a voxel's preferred (most coherent) X and Y coordinates in the visual field can be estimated.*

## 2.3. Stimuli

The polar mapping stimuli used here was a rotating thin wedge with the apex at the fixation point (see Figure 16A). Eccentricity mapping consisted of an annulus either expanding from or contracting towards the fixation point (see Figure 16B). All visual stimuli were composed of high-contrast light and dark coloured regions alternating counterphase at a rate of 8 Hz. Both stimuli conditions had a reverse direction complement in order to help correct for haemodynamic lag (Sereno et al., 1995).

A B

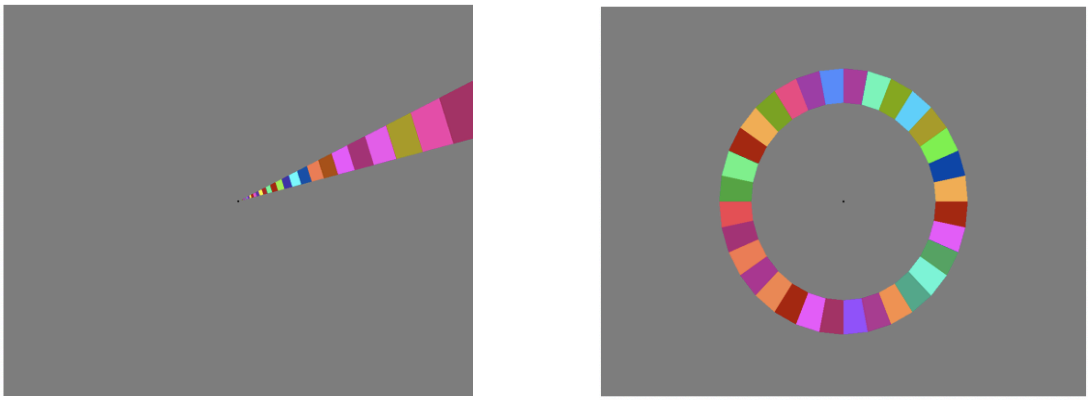


*Figure 16. The polar (left) and eccentricity (right) mapping stimuli used in this thesis. The polar mapping wedge stimulus rotates 360°around the central point (both clockwise and counter-clockwise versions of the stimuli were used). The annulus used for mapping eccentricity expands from the central fixation point, eventually reaching the far periphery (both expanding and contracting versions of the annulus were used). The high-contrast light and dark coloured regions alternating counterphase at a rate of 8 Hz.*

## 2.4. Scanning

For each participant, the retinotopic mapping data were acquired in a single session consisting of four polar angle scans (two clockwise, two counter-clockwise) and two eccentricity scans (one expanding, one contracting). The bottom part of a Siemens 32-channel head coil was raised and tilted so the participant's head was at an angle where they could view a frosted glass in-bore projection screen, positioned at a distance of ≈10cm from the participant's eyes. At this distance participants could comfortably focus on a small fixation cross at the centre of the screen, while allowing the stimuli to extend to the periphery of their vision. Participants were required to maintain fixation throughout the period of scan acquisition. The participant's head was also stabilized with foam pads to reduce head movement. Polar angle and eccentricity visual stimuli subtended a maximum visual angle 35° wide and 26° tall.

Echo-planar images were collected on a Siemens 1.5T MRI scanner at the Birkbeck-UCL Centre for Neuroimaging (BUCNI) using only the bottom 20 channels of a standard Siemens 32-channel head coil. Removing the top 12-channels gave participants an unobstructed view of the stimuli and primarily affected sensitivity to frontal brain regions; sensitivity in posterior areas of the brain including striate and extrastriate visual regions was still high. Gradient-echo echo-planar images were collected as the participants passively viewed the stimuli (3.2 x 3.2 x 3.2mm, 24 slices, TR=2s, TE=39ms, 1474 MHz bandwidth, 262 volumes – 6 of which were dummy volumes to allow for T1 equilibrium). After three or four runs, a whole-brain 'alignment scan' was acquired using an T1-weighted MPRAGE sequence (TR = 1000 ms, TI =

8.4 ms, TE = 3.57 ms, flip angle = 7°, matrix = 224 × 256, 176 axial slices, 1 × 1 × 1

mm voxels) aligned to the functional slices used in the polar angle mapping. This was used to establish an initial registration of the functional data with the structural alignment scan which facilitated the final surface-based mapping. In a separate scanning session, two T1-weighted MRI images (MPRAGE, 1 × 1 × 1 mm, 10mins each) were acquired with the full 32-channel head-coil in place. These structural scans were used for surface reconstruction. The four polar angle scans, two eccentricity scans, the alignment scan, and the two high resolution structural scans required a total of 75 minutes of scan time per person.

## 2.5. Analysis

Retinotopy image processing was carried out using Freesurfer (http://ftp.nmr.mgh.harvard.edu/). The two high-resolution T1-weighted images were skull stripped, averaged together, and then used to compute the cortical surface. This involved segmenting the white and grey matter. This segmentation was visually inspected and confirmed in each participant (see Figure 17A). Once verified, the grey matter was 'inflated' (using a mesh flattening algorithm) to create a surface for inspecting the retinotopic mapping that was not obscured by cortical folding (see Figure 17B).

*A*

*B*

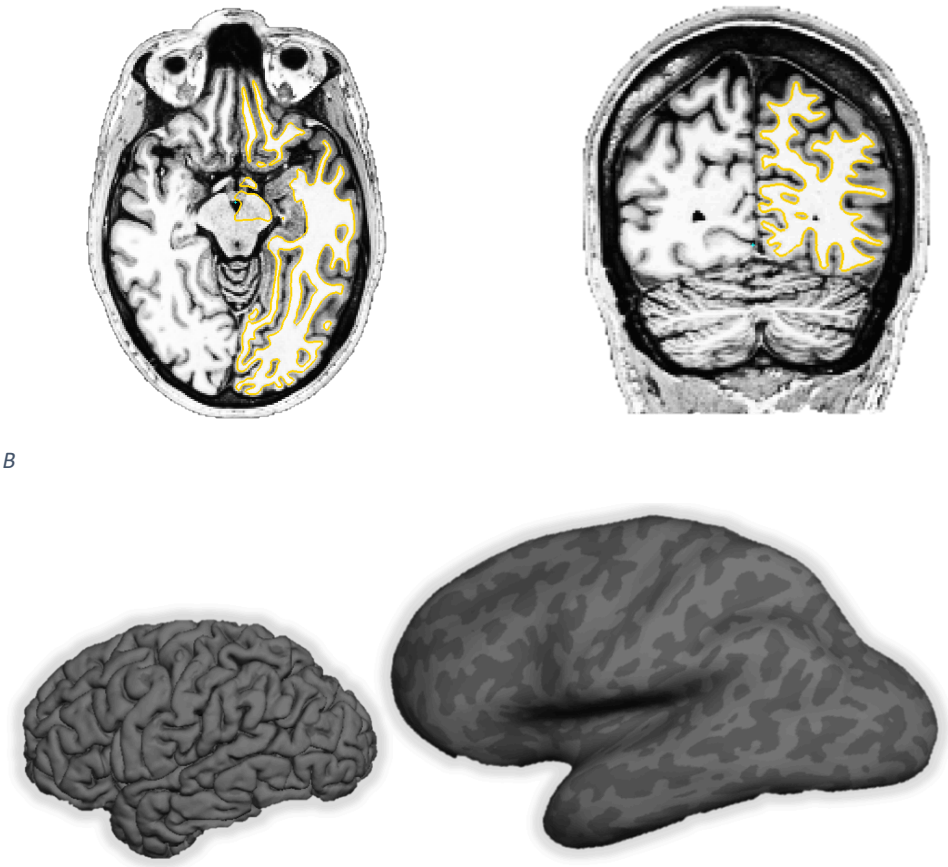


*Figure 17. Grey matter Segmentation and inflation. (A) Results of the automated segmentation of white/grey matter shown on a participant's anatomical scan. (B) The grey matter surface of the left hemisphere (left panel) inflated using mesh flattening algorithm. The Inflated surface (right panel) exposes the sulcal regions and makes it easier to identify and draw the borders of the visual ROIs.*

Volumes in the functional polar and eccentricity scans were aligned to the centre volume in the sequence to reduce the effects of small head movements. Each participant successfully completed the 6 scans.

The centre volume of the time series was then manually registered to the T1-weighted alignment scan that was in the same plane as the functional scans. Next, the alignment scan was manually registered to the high resolution structural scan. By concatenating these mappings, the functional data were then projected on to the cortical surface. After removing the first six volumes to allow for T1-equilibrium to be reached, the four polar scans and two eccentricity scans were Fourier-analyzed. Individual first level analyses were combined into polar and eccentricity averages and then smoothed with a 3mm FWHM kernel in two dimensions on the cortical surface.

The resulting maps were visually consistent with those reported in Sereno et al (1995). As can be seen in Figure 18, the most central, foveal representations (red) are situated near the occipital pole with eccentricity progressively increasing through parafoveal (blue) and peripheral coverage (green) moving anteriorly along the cortical surface. On the polar angle map (see Figure 19), the horizontal meridian (blue) is situated approximately over the calcarine sulcus and divides representations of the upper and lower quadrants of the visual field. Moving from the calcarine sulcus ventrally along the surface, coverage transitions to the upper visual field (red). Moving dorsally, coverage transitions to the lower visual field (green).

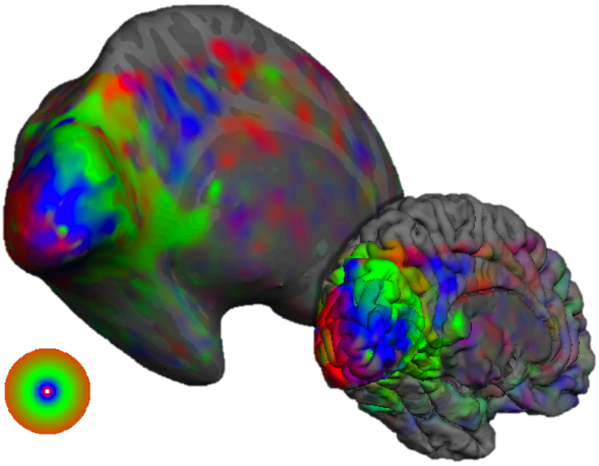


*Figure 18. Eccentricty mapping overlaid on a participant's uninflated (right) and inflated (left) cortical surfaces (both left hemisphere). Isoeccentricity is coded by colour: red for fovea, blue/green for parafovea, and yellow/red for the periphery. As can be seen, there is a large foveal representation near the occipital pole with eccentricity progressively increasing through parafoveal (blue) and peripheral coverage (green) moving anteriorly along the cortical surface*

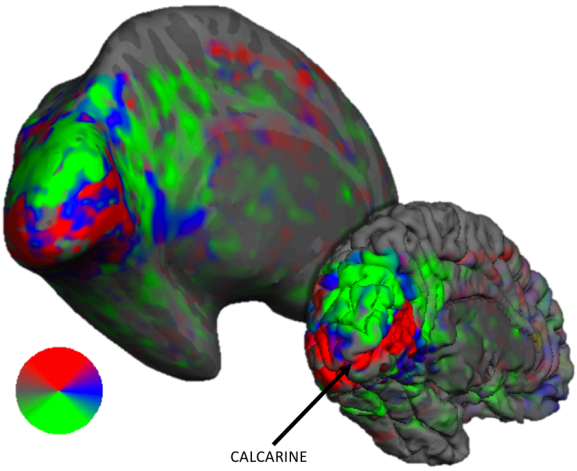



*Figure 19. Polar mapping overlaid on a participant's uninflated (right) and inflated (left) cortical surfaces (both left hemisphere). Isopolar is coded by colour: red for upper vertical meridian, blue for horizontal meridian, and green for lower vertical meridian. As can be seen, the cortex above (dorsal) the calcarine represents the lower visual field and the cortex below (ventral) represents the upper visual field.*

## 2.6. Cutting and flattening of occipital patches

To make it easier to identify and draw the borders of the visual areas, a portion of the occipital lobe was cut from the inflated cortical surface and flattened. As shown in Figure 20, the first cut was made along the fundus of the calcarine sulcus. At the anterior end of the sulcus, a second, perpendicular cut was made that continued all the way around the surface, separating the occipital lobe from the rest of the brain. The separate occipital surface was then flattened.

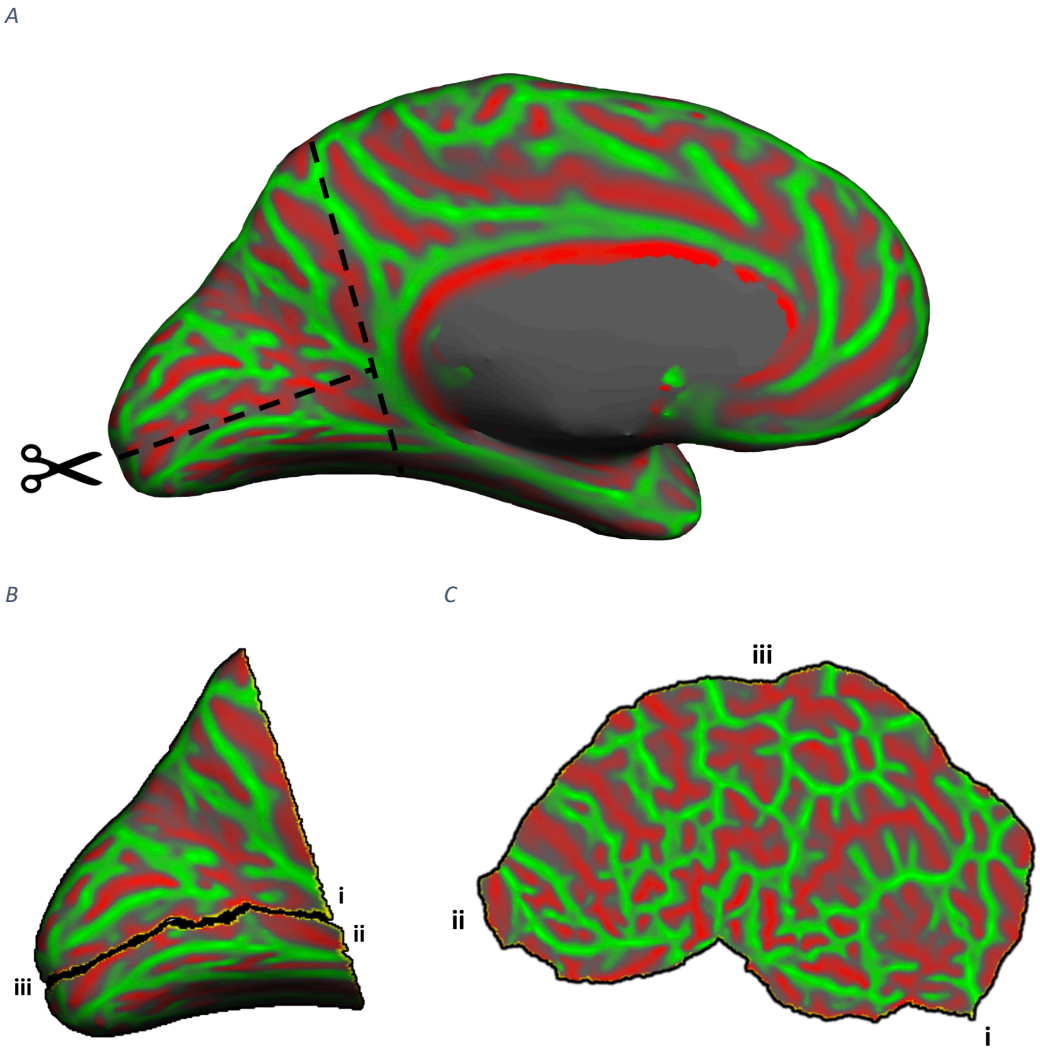



*Figure 20. Cutting and flattening occipital patches. (A) Occipital patches (bottom right) were created by making perpendicular cuts along the cortical surface. The posterior-anterior cut was centered on the fundus of the calcarine fissure. (B) The detached occipital surface after cutting. (C) The flattened occipital surface. Gyri and sulci are represented by green and red colours respectively.*

## 2.7. Drawing the borders for the visual areas

*V1, V2, and V3*

Areas V1, V2, and V3 have complete maps of the contralateral hemifields and their borders were drawn (on the occipital patches) according to reversals in the polar representations (see Figure 21). I defined V1 as starting at the representation of the horizontal meridian near the fundus of the calcarine sulcus and extending to the nearest representations of the upper and lower vertical meridians (moving ventrally and dorsally respectively). V1 shares a

border with V2 at the point where this vertical representation reverses and begins to transition back toward the horizontal meridian. I defined V2 as extending from this shared representation of the vertical meridian with V1 to the nearest representation of the horizontal meridian. V2 shares a border with V3 at the point where this horizontal meridian representation reverses and begins to transition toward the vertical meridian. I defined V3 as extending from this shared horizontal representation with V2 of the nearest mid-point of the vertical meridians. Once the borders were marked, I created volumetric masks for V1, V2, and V3 for each participant in their anatomical space.

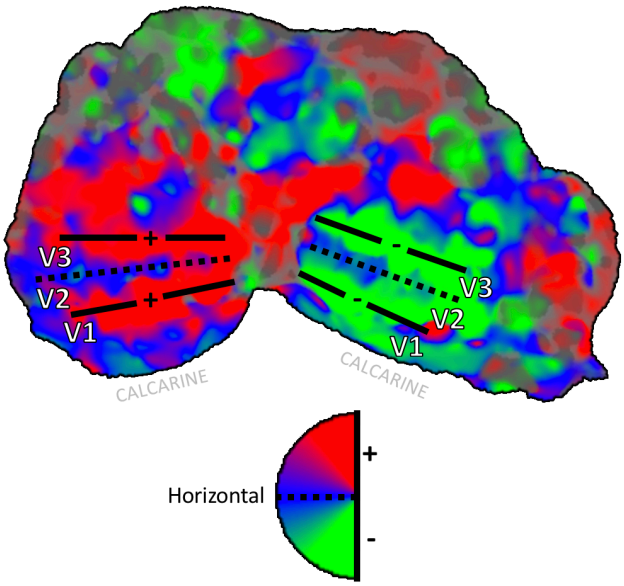



*Figure 21. Polar angle retinotopic map shown on an inflated and flattened left hemisphere occipital surface of one of the participants. Areas V1, V2, and V3 were drawn according to the reversals in their polar representations. The V1 visual field map extends from the horizontal meridian (near fundus of the calcarine sulcus; labelled CALCARINE in this figure), to the upper and lower vertical meridians (on the ventral and dorsal surfaces respectively; the upper vertical meridian is denoted by "+" and the lower vertical meridian by a "-"). V2 and V1 share a border where a reversal begins in the representation of visual angle. V2 extends from this shared representation of the vertical meridian to the horizontal meridian where it shares a border with V3 at the point where another reversal begins. V3 extends from this shared representation of the horizontal meridian to the vertical meridian*

Within V1, V2, and V3 I also defined two sub-regions of interest (see Figure 22). The central (stimulated) sub-region included cortex with coverage of the visual field between 0-3.8$^{o}$ visual angle, a range that comfortably encompassed the visuotopic extent of the stimuli (that had a maximum width subtending 1.7$^{o}$ visual angle). The peripheral (non-stimulated) sub-region included the remaining cortex representing >3.8$^{o}$ in the visual field.

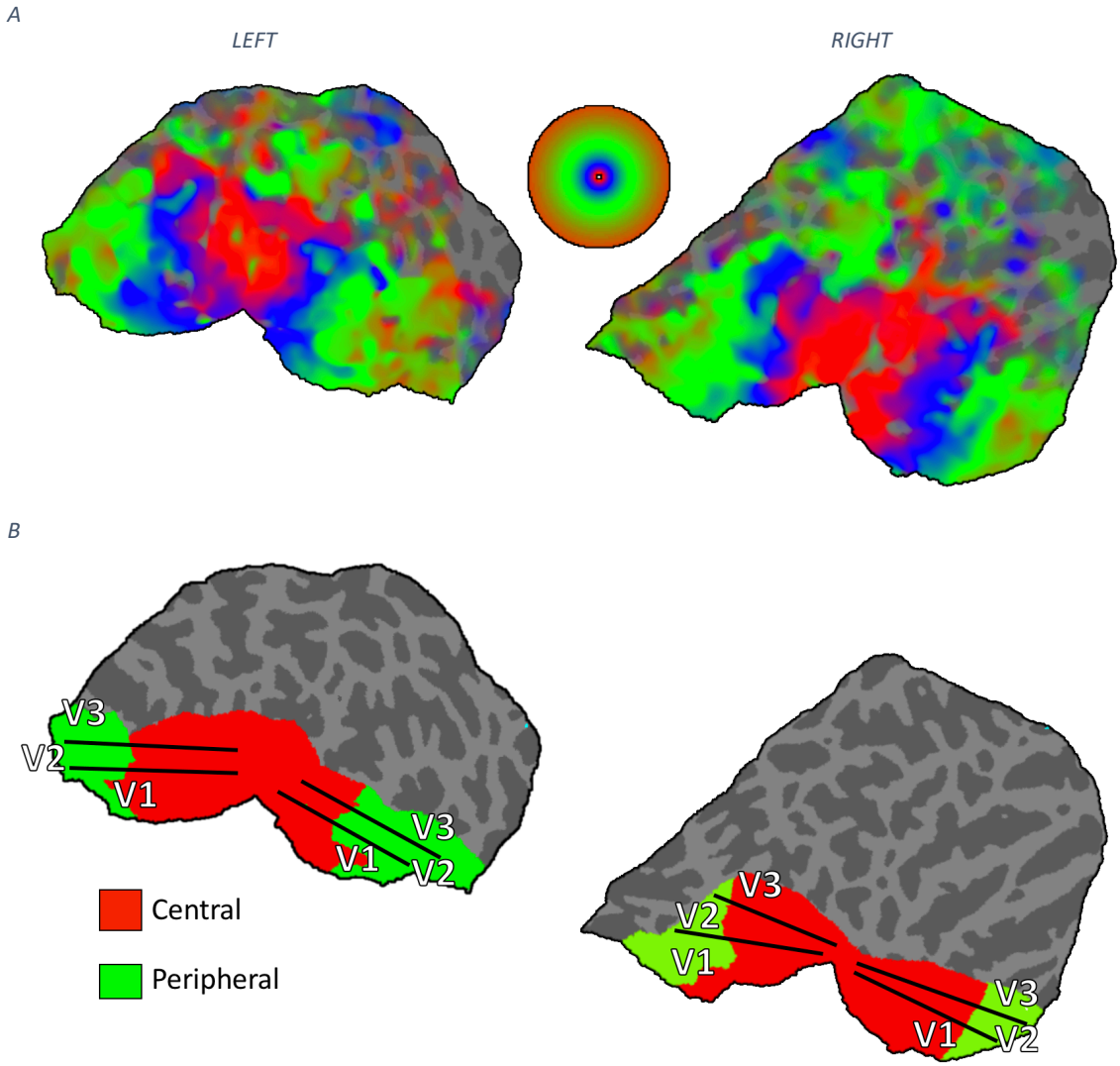



*Figure 22. The Central and Peripheral regions of interest. (A) Eccentricity retinotopic maps were used to define the central and peripheral ROIs in areas V1, V2, and V3. The central ROI was defined as cortex representing the foveal and parafovea regions of the visual field (up to 3.8° visual angle). The peripheral ROI included the remaining cortex representing the periphery of the visual field (beyond 3.8° visual angle). (B) one participant's central (red) and peripheral (green) ROIs in V1, V2, and V3 shown on their flattened left and right hemisphere occipital surfaces.*

*Ventral areas V4, VO1, VO2, and VOT*

I divided the ventral surface into V4, VO-1, and VO-2 ROIs (see Figure 23) using the hV4/VO criteria (Wandell et al., 2005; Wandell et al., 2007). Accordingly, I defined hV4 (hereafter V4) as a hemifield representation that shared a border with ventral V3 (at the representation of the upper vertical meridian) and extended anterior-laterally to a representation of the lower vertical meridian. Adjacent to the anterior aspect of V4, I defined two other hemifield ROIs,

VO-1 and VO-2, that also shared a border with the ventral aspect of V3. From this border, I defined these as extending ventral-laterally into a distinct foveal representation, near inferior occipital gyrus, that is ventral and anterior to foveal confluence. This distinct foveal representation was apparent in all participants. I defined the posterior border of VO-1 both by referencing the midpoint between the lower vertical meridian shared with V4 and according to the reversal in eccentricity found near the onset of the peripheral representation. I defined the anterior border of VO-1, that is shared with VO-2, at the mid-point in the representation of the vertical meridian. In one participant's left hemisphere, the division between V4/VO-1 was difficult to discern so I used additional anatomical criteria to draw the border. Specifically, in most participants, the V4/VO-1 border is located at the posterior transverse collateral sulcus (Witthoft et al., 2014). I used this landmark to draw this participant's V4/VO-1 border. After drawing borders of the three ventral visual ROIs, I also defined a VOT ROI in both hemispheres. The VOT is largely unresponsive to standard retinotopic mapping procedures so the borders were specified using standard coordinates (Twomey et al., 2011). In all participants, the retinotopically defined areas VO-1 and VO-2 abutted the VOT (see Figure 23) which is consistent positioning with previous studies (Rauschecker, Bowen, Parvizi, & Wandell, 2012; Yeatman, Rauschecker, & Wandell, 2013).

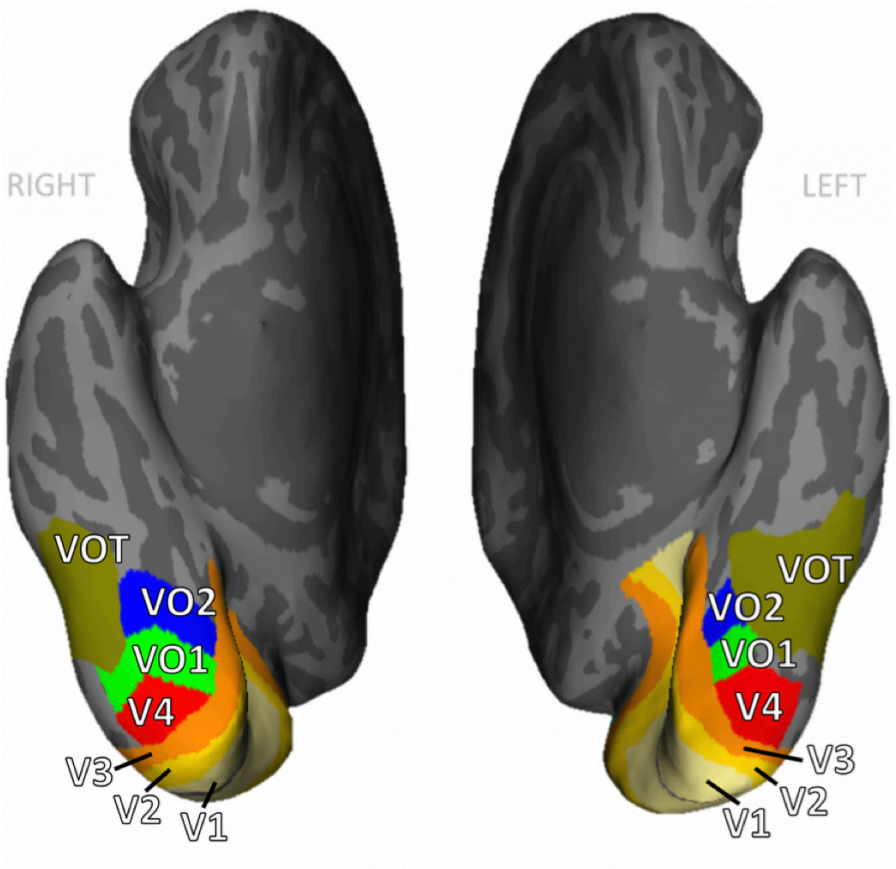



*Figure 23. Retinotopically defined areas V4, V-O1, V-O2 on inflated left (left side) and right (right side) hemispheres. The VOT was defined using standard coordinates (Twomey et al., 2011). Areas V1, V2, and V3 also shown.*

*Dorsal areas V3A, V3B, and V7*

I divided the dorsal surface into V3A, V3B and V7 ROIs using the criteria described by Larsson and Heeger (2006). Accordingly, I defined V3A and V3B as adjacent field maps with complete polar representations of the contralateral hemifield that extended from the shared border with anterior V3d (at a representation of the lower vertical meridian) to the nearest upper vertical meridian representation that is also the anterior border of V7. I defined V7 as extending from this border to the midpoint in the nearest representation of the horizontal meridian. Like VO maps in the ventral areas, the eccentricity representation for these dorsal areas are not aligned with the central confluence and instead include a small, distinct foveal representation that is typically found within the transverse occipital

sulcus at the base of the intraparietal sulcus (Wandell et al., 2007). I defined the border between V3A/B as the eccentricity mid-point in their shared foveal representation. In one participant, the eccentricity maps were indistinct in the dorsal region around V3A/B and V7 so identification was aided by the anatomical reference point of the transverse occipital sulcus. Even though the foveal representation of V3A/B was not clearly defined in this participant, eccentricity representations extending in opposite directions could be discerned so I could make a good estimate of the midpoint border. Because borders could be reasonably identified in all participants, V3A and V3B were defined as separate areas rather than as single complex.

*Area V5*

In most participants, the distinct foveal representation V5 can readily be found on occipital patches at about the same dorsoventral level as the central confluence but clearly separated by a region of larger eccentricities (Tootell & Hadjikhani, 2001). Following the criteria described by Kolster (2010), I defined V5 as a complete hemifield map centred on this foveal region and extending from a representation of lower vertical meridian at the posterior end (i.e. toward V3) to an upper vertical meridian at the anterior end.

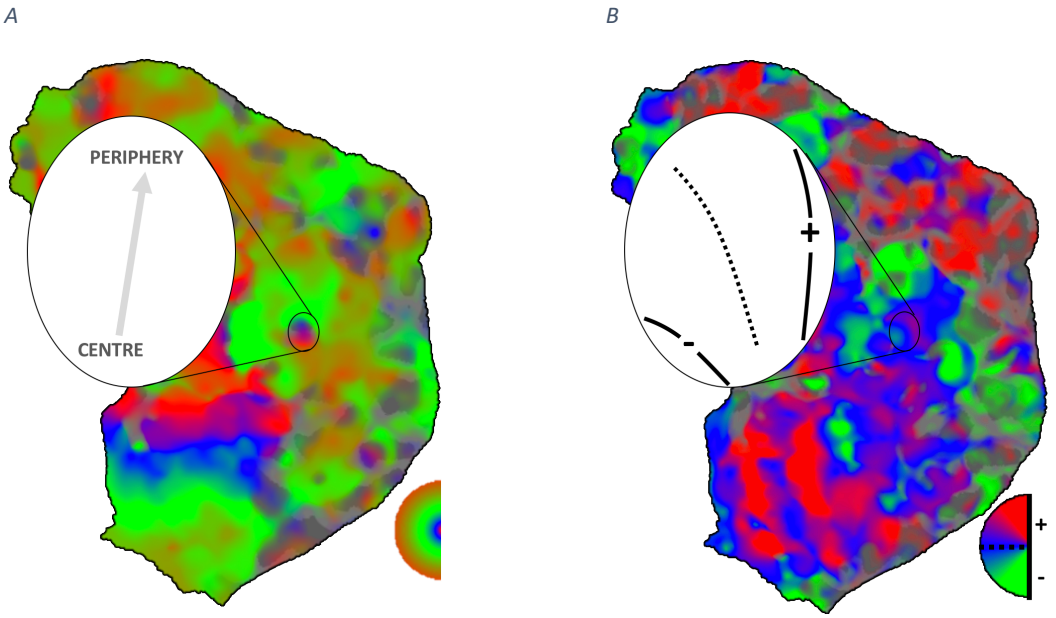



*Figure 24. V5 drawn on a participants's flattened occipital patch (right hemisphere). (A) V5 was defined as complete hemifield map centred on a foveal region that was inline (dorsoventral) with the central confluence but separated by a region of larger eccentricities (green). Eccentricity representation extended from the centre to the periphery. (B) The polar representation extended from the lower vertical meridian (solid line with minus sign), through the horizontal meridian (dashed-line), to upper vertical meridian (solid line with plus sign).*

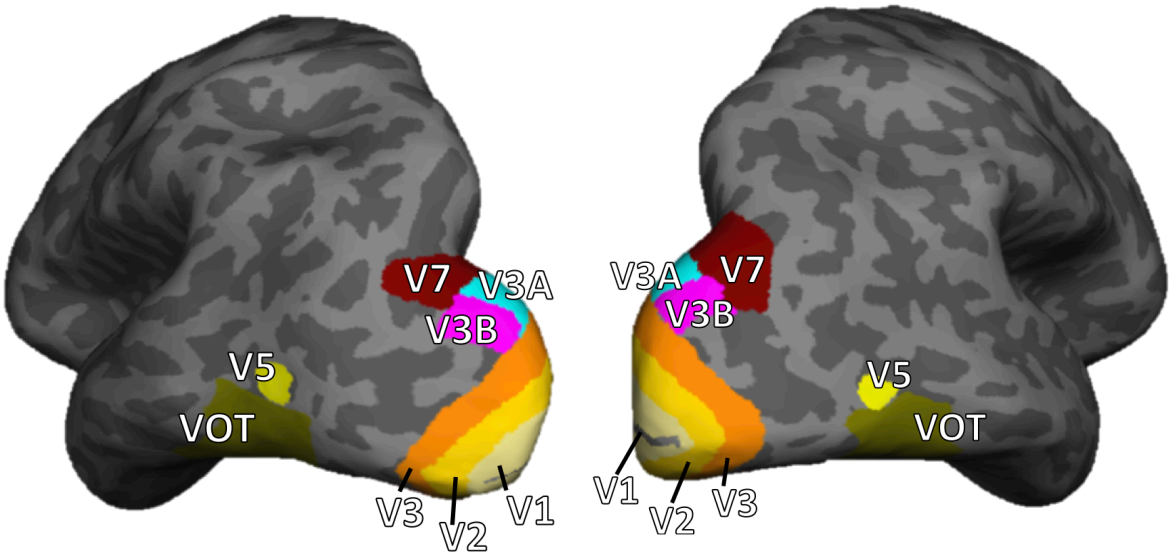



*Figure 25. The dorsal ROIs V3A, V3B, V7 and area V5 shown on a participant's inflated left and right hemispheres (left and right panels respectively). V1, V2, V3, and VOT ROIs also shown*

## 2.8. Reading tasks

Investigating how the visual ROIs are involved in reading required methods capable of distinguishing bottom-up visual signals from top-down linguistic (or other higher-order processing) components. To address this requirement, I used several different reading tasks, each designed to emphasize a different aspect of reading, while keeping the stimuli the same across the tasks so I could separate stimuli-bound responses from processing-bound responses. In addition, I manipulated the stimuli to incorporate a range of linguistic factors important to reading while maintaining tight control over low-level differences in visual form that the early visual areas in particular will be highly sensitive to. Unlike the few previous investigations into the early visual stages of reading that also used other visual forms like basic shapes, symbols, and simple line drawings (Petersen et al., 1990; Tarkiainen et al., 1999; Vinckier et al., 2007; Wise et al., 1991), my experiments used only letter string stimuli. Mixed stimuli sets that include non-letter stimuli are useful for identifying where sensitivity to written language first emerges relative to those visual controls, but these contrasts all but factor out the early stages of visual processing. In the present experiments, the stimuli were entirely composed of letters from the English alphabet arranged into 4-5 letter combinations. From the perspective of low-level visual features, the stimuli were highly controlled to allow the neural activity related to the ascending spatial processing to be held constant across conditions as higher-order properties (like whether the letter arrangements form a word or not) change.

## 2.9. Stimuli

There were four stimuli conditions: consonant letter strings, orthotactically-legal pseudowords, low frequency English words, and high frequency English words. Each condition had 150 stimuli consisting of 4-5 character strings of English letters.

- *Consonant Strings* (CS) items were pseudo-random arrangements of consonants that lacked phonological or semantic information (e.g. 'cchw'), and therefore provided a useful baseline condition. Because they used the same character set as the other conditions, vowels aside, they are highly comparable in terms of visual form and complexity.
- *Pseudowords* (PW) were arrangements of letters that respected English orthotactic and phonotactic restrictions without forming actual words in English (e.g. 'cavel'). As a result, they were pronounceable but had no meaning.
- *Low Frequency* (LF) and *High Frequency* (HF) words were all valid English words that differed in how frequently they occur in British English use. Items from both conditions were drawn from the MRC Psycholinguistic database (Coltheart, 1981) and all had a rated familiarity above 400. High frequency words had a frequency of 40 or more per million while low frequency words had a frequency of 20 or less per million in British English use (Baayen, Piepenbrock, & Gulikers, 1995).

Word frequency is among the most extensively studied variables in psycholinguistics and people have repeatedly been shown to respond faster to high frequency than to low frequency words (Balota, Yap, & Cortese, 2006; Balota, Yap, & Hutchison, 2012). The wide

range of cortical areas affected by this variable suggests that it does not affect only a single aspect of word processing. As a result, it is a useful parameter for revealing core language areas involved in word recognition. A summary of the stimuli characteristics is shown in Table 1.

| | CS | PW | LF | HF |
|---|---|---|---|---|
| Letter length | 4.5 (+/- 0.5) | 4.5 (+/- 0.5) | 4.5 (+/- 0.5) | 4.5 (+/- 0.5) |
| Frequency (per million) | – | – | 8 (+/- 6) | 162 (+/- 149) |
| Number of syllables | – | 1.2 (+/- 0.4) | 1.2 (+/- 0.3) | 1.2 (+/- 0.4) |
| Orthographic neighbourhood (N) | – | 6.2 (+/- 4.6) | 6.1 (+/- 4.3) | 6.0 (+/- 4.6) |
| Bigram frequency | – | 1619 (+/-1109) | 1727 (+/-1502) | 1728 (+/- 1394) |
| Trigram frequency | – | 280 (+/- 333) | 311 (+/- 359) | 361 (+/- 365) |
| Imageability | – | – | 511 (+/- 72) | 508 (+/- 85) |
| Concreteness | – | – | 485 (+/- 107) | 475 (+/- 99) |

*Table 1. Average values for 8 stimuli properties in each of the four conditions (Constant strings (CS), Pseudowords (PW), Low Frequency Words (LF), and High Frequency Words (HF)). As can be seen above, other than Frequency, the properties were well-matched across the conditions. Frequency was intentionally manipulated to form a set of high frequency words (HF) and low frequency words (LF). Standard deviation shown in parentheses.*

## 2.10. Control of stimuli properties

Psycholinguistics has identified several important lexical and sub-lexical properties that impact of visual word recognition performance although, importantly, the effect of these

properties can be task dependent. For example, orthographic neighborhood size has been demonstrated to decrease reaction times in in lexical decisions tasks (Andrews, 1997) and increase them in semantic tasks (Forster & Shen, 1996). To help avoid confounds and focus the experimental manipulation on the condition contrasts outlined above, care was taken to control for the following key factors that have been widely implicated in reading task performance.

*Number of Syllables*

In the lexical decisions task, the number of syllables in a word (even after controlling for other factors) has been shown to be positively correlated with response time (Yap & Balota, 2009) and this variable may have a different impact on non-word items (Ferrand and New, 2003). Consequently, pronounceable stimuli (i.e. low & high frequency words and pseudowords) ranged from 1-3 syllables and were matched across conditions (see Table 2 and Table 3).

*Orthographic Neighborhood Size*

Orthographic neighborhood size (N) can be calculated for both words and non-words and is defined as the total number of words that can be formed by swapping a single letter for another. A standard finding (in the lexical decisions task) is that participants respond faster to words with a high N compared to those with small neighborhoods (Andrews, 1997; Forster & Shen, 1996). In contrast, for pseudowords the evidence suggests that subjects take longer to respond (i.e. reject) if the stimuli have a large N (Balota, Cortese, Sergent-Marshall, Spieler, & Yap, 2004; Forster & Shen, 1996). Consequently, N was matched across the two word and one pseudoword conditions (see Table 2 and Table 3).

*Bigram and trigram frequency*

The frequencies of two- and three-letter combinations (bi- and trigrams) in words and non-words have only occasionally been shown to affect word recognition performance (Broadbent & Gregory, 1968; Rice & Robinson, 1975). Even so, this factor is important because the LCD model of visual word recognition specifies that bigrams and trigrams form an important level of representation at the neural level (Cohen et al., 2002; Dehaene et al., 2005; Vinckier et al., 2007). To avoid potential confounds, both were matched across the two word and one pseudoword conditions (see Table 2 and Table 3).

*Imageability and concreteness*

Imageability is the ease to which a word can evoke a visual image. Concreteness refers to a concept's physicality – concrete objects can be touched while abstract objects cannot. These two factors, imageability and concreteness, are conceptually related and highly correlated yet distinct enough to warrant separate controls. In lexical decision tasks, subjects have been shown to respond faster and more accurately to high-imageability than low-imageability concepts (Balota et al., 2004) and to concrete relative to abstract concepts (Binder, Westbury, McKiernan, Possing, & Medler, 2005; Gernsbacher, 1984; Howell & Bryden, 1987; James, 1975; Whaley, 1978). Further, concrete words have been found to be more resilient than abstract words to brain damage (Katz & Goodglass, 1990; Roeltgen, Sevush, & Heilman, 1983). As both of these are semantic factors, they only apply to the low and high frequency word conditions (and not to the non-word conditions). All words were chosen to have minimum imageability and concreteness ratings of 311 and 267 respectively

based on the MRC Psycholinguistic database (Coltheart, 1981) and were balanced across LF and HF word conditions (see Table 2).

Each stimuli condition was divided into 5 lists of 30 items each. Words were matched across conditions and lists using a 2 × 5 ANOVA with Frequency (low, high) and List (1-5) as independent measures. Dependent measures included number of letters, number of syllables, orthographic neighbourhood size (N), bigram frequency, trigram frequency, rated imageability, and rated concreteness. The purely orthographic values (namely, N, bigram and trigram frequency) come from the N-watch program and were based on British English spellings (Davis, 2005). All other values were taken from the MRC Psycholinguistic database (Coltheart, 1981). There were no significant main effects of Frequency or List, nor any significant interactions for these factors (see Table 2), indicating that the five lists were well matched across these measures. By definition, there was a significant main effect of written word frequency ($F(1,290)=157.6$, $p<0.001$). Finally, there were non-significant trends towards a main effect of List ($p=0.06$) and a Frequency×List interaction ($p=0.07$).

| | MAIN EFFECTS | | |
|---|---|---|---|
| WORD PROPERTY | FREQUENCY | LIST | FREQ *LIST |
| Concreteness | 0.02 | 0.12 | 0.69 |
| Imagineability | 0.07 | 0.31 | 0.31 |
| Number of Letters | 0.33 | 0.60 | 0.66 |
| Number of Syllables | 0.70 | 1.51 | 0.85 |

| | | | |
|---|---|---|---|
| Bigram Frequency | 0.00 | 1.15 | 0.89 |
| Trigram Frequency | 1.28 | 0.83 | 1.73 |
| Orthographic N | 0.05 | 1.00 | 0.72 |
| Celex (Word Frequency) | 157.56* | 2.26 | 2.18 |

*Table 2. Low Frequency and High Frequency words (in all five lists) were matched on lexical and sub-lexical properties. The table above shows the F values for each of those properties following a 2 × 5 ANOVA with Frequency (low, high) and List (1-5) as independent measures. *The main effect of Frequency confirms the difference between the two categories of words.*

The non-word stimuli (i.e. PW and CS) were created to match the word stimuli as closely as possible. Pseudowords and words were matched across conditions and lists using a 3 × 5 ANOVA with Condition (PW, LF, HF) and List (1-5) as independent measures. Dependent measures included number of letters, number of syllables, orthographic neighbourhood size (N), bigram frequency, trigram frequency. As shown in Table 3, the number of letters, number of syllables, bigram frequency, or trigram frequency, and orthographic neighborhood size did not differ significantly between conditions. Consonant strings were also matched on the number of letters with a 4 × 5 ANOVA with Condition (PW, LF, HF, CS) and List (1-5) as independent measures confirming that there were no main effects of length on Condition ($F(3,580)=0.56$), List ($F(4,580)=0.74$) and no significant List × Condition interaction ($F(12,580)=0.41$).

| | MAIN EFFECTS | | |
|---|---|---|---|
| WORD PROPERTY | FREQUENCY | LIST | FREQ *LIST |
| Number of Letters | 0.17 | 0.47 | 0.47 |
| Number of Syllables | 0.40 | 0.97 | 0.74 |
| Bigram Frequency | 0.35 | 1.25 | 0.73 |
| Trigram Frequency | 2.01 | 1.00 | 1.18 |
| Orthographic N | 0.07 | 0.51 | 0.73 |

*Table 3. Pseudowords, Low Frequency, and High Frequency words (in all five lists) were matched on lexical and sub-lexical properties. The table above shows the F values for each of those properties following a 3 × 5 ANOVA with Frequency (pseudo, low, high) and List (1-5) as independent measures. All p-values ≥ 0.14.*

## 2.11. Tasks

Many studies show that brain activity during reading tasks depends not just on the written stimuli, but also on the specific task demands (Carreiras, Mechelli, & Price, 2006; Chee, Hon, Caplan, Lee, & Goh, 2002; Kuperman, Drieghe, Keuleers, & Brysbaert, 2013; Schilling, Rayner, & Chumbley, 1998). I used four commonly used reading tasks, each designed to emphasis a different aspect of reading, and a test of working memory to try to tease apart processing-related brain activity from activity linked directly to the written stimulus.

| | | RESPONSE | | |
|---|---|---|---|---|
| TASK | DECISION | BUTTON | REQUIRED | CONDITION |
| Covert Reading | – | – | – | LF, HF, PW, CS |
| Lexical Decisions | Is an English word? | "Yes"/"No" | Every trial | LF, HF, PW, CS |
| Phonological Decisions | Is it a rhyme of "true"? | "Yes" | Target trials | LF, HF, PW |
| Semantic Decisions | Is it the name of a country? | "Yes" | Target trials | LF, HF |
| One-back | Is repeat of the last stimuli | "Yes" | Target trials | LF, HF, PW, CS |

*Table 4. Task requirements including the decisions required, the button press required (if applicable) and whether a response was required on every trial (Lexical Decisions) or only when a target was detected. The conditions used in each task are also listed.*

*Covert Reading*

The covert reading task required participants to read the words silently to themselves. It was included not only because of its ecological validity but, as the only task that doesn't require a response, it provides a useful control over potential response factors in the neural response. The task included all four stimuli conditions and required participants to silently read the pronounceable stimuli (e.g. "cloth") or covertly say "OK" when they encountered consonant strings (e.g. "gkcc"). There was a total of 600 stimuli (4 conditions $\times$ 150 stimuli).

*Lexical Decisions*

The lexical decision task required participants to make a yes/no response to whether a stimulus was a valid English word or not. The lexical decision task is widely regarded as a measure of lexical access and processing (Jacobs & Grainger, 1994) and has been widely applied in neurolinguistics research (Fiebach, Friederici, Muller, & von Cramon, 2002; Heim,

Eickhoff, Ischebeck, Supp, & Amunts, 2007; Perani et al., 1999; Xiao et al., 2005). In the current investigation, the lexical decisions required participants to respond, on every trial, with a "yes" button press if the stimulus was a valid English word and the "no" button press otherwise. Response times and accuracy were recorded for each trial. Task stimuli included all four conditions (CS, PW, LF, HF) yielding equal numbers of yes and no trials. There was a total of 600 trials (4 conditions $\times$ 150 stimuli). Based on recent psycholinguisitic 'mega studies' of 10,000+ subjects (see Balota et al., 2006; Balota et al., 2012 for a review), I predicted that participants will respond fastest for consonant strings and slowest for pseudowords. In addition, I expect a robust word frequency effect, with significantly faster responses to high frequency than to low frequency words.

*Phonological Decisions*

Phonological decisions required participants to respond whenever a stimulus rhymed with "true". Phonological decision tasks are designed to focus attention on the sounds of words and come in many forms including syllable decisions (Gabrieli, Poldrack, & Desmond, 1998; Poldrack et al., 1999; Price, Moore, Humphreys, & Wise, 1997), phoneme tasks (Raizada & Poldrack, 2007), and rhyme judgments (Pugh et al., 1997). Previous studies using tasks that emphasize phonological processing have found strong engagement of not only vOT, but also the supramarginal gyrus (Petersen et al., 1988; Raizada & Poldrack, 2007; Seghier et al., 2004; Yoncheva et al., 2010; Zevin & McCandliss, 2005) and posterior aspects of Broca's area (Buckner et al., 1995; Fiez, 1997). Here I used a rhyme detection task that required participants to press the "yes" button if the stimulus rhymed with "true." There was no response for stimuli that did not rhyme with "true." All the pronounceable conditions were included (PW, LF, and HF) but unpronounceable consonant strings were omitted. In addition

to the set of 150 items per condition, an additional 20 target stimuli were created for this task (4-5 character rhymes such as “blue”) for a total of 550 trials (3 conditions × 150 stimuli + (20 targets × 5 task runs)). See the Appendix for a complete list of the target words.

*Semantic Decisions*

Semantic decisions required participants to press the “yes” button if the stimulus was the name of a country (e.g. “Syria”). Semantic decision tasks are designed to focus attention on the meaning of words. Previous studies using tasks that emphasize semantic processing have found strong engagement of not only vOT but also the anterior temporal lobes (Visser, Jefferies, & Lambon Ralph, 2010), anterior and ventral aspects of Broca’s area (Buckner et al., 1995; Devlin, Matthews, & Rushworth, 2003; Fiez, 1997), and angular gyrus (Binder et al., 2009). The current task required 20 additional target stimuli consisting of 20 country names (all 4-5 letters, see the Appendix for a complete list of the countries). Because nonwords do not have any specific meaning, only low and high frequency words were included in this experiment for a total of 400 trials (2 conditions × 150 stimuli + (20 targets × 5 runs)).

*One-back*

The one-back task required participants to respond whenever a stimulus repeated. *N*-back tasks are widely used in cognitive neuroscience to investigate working memory (see Owen, McMillan, Laird, & Bullmore, 2005 for examples). Unlike the other four tasks, the one-back task is not classically considered a reading paradigm and is the only task that could be successfully performed purely orthographically (that is, without recognizing the stimulus). I included it, even so, because it is frequently used to localize ‘reading-specific’ brain areas

(Centanni et al., 2018; Diehl et al., 2014; Szwed et al., 2011). Because its task-demands differ so markedly from the reading tasks, it provides a strong test of how much activation is driven purely bottom-up (i.e. stimulus-driven) vs. top-down (processing-driven). The one-back task in the current investigation required participants to press a "yes" button if the stimulus was identical to the stimulus presented in the trial immediately before. Unlike the other four tasks, the one-back task could be successfully performed using only orthographic information (that is, without recognizing the stimulus). Response times and accuracy were recorded for each target trial (i.e. trials where the stimuli were identical to the previous trial). All four stimuli conditions were included in the task for a total of 680 trials (4 conditions × 150 stimuli + (16 repeated (i.e., target) items × 5 task runs).

| | CONDITIONS | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| TASK | CS | PW | LF | HF | TARGETS | TRIALS | RUNS | TOTAL |
| Covert Reading | 30 | 30 | 30 | 30 | – | 120 | 5 | 600 |
| Lexical Decisions | 30 | 30 | 30 | 30 | – | 120 | 5 | 600 |
| Phonological Decisions | – | 30 | 30 | 30 | 20 | 110 | 5 | 550 |
| Semantic Decisions | – | – | 30 | 30 | 20 | 80 | 5 | 400 |
| One Back | 30 | 30 | 30 | 30 | 16* | 136 | 5 | 680 |

*Table 5. Task stimuli. Asterisk (*) denotes that in the one-back task, the target trials were duplicates of stimuli in the 5 stimuli lists for each condition.*

Participants performed the tasks in the scanner, lying supine with the stimuli projected onto a frosted glass screen at the front of the scanner bore and viewed via mirrors attached to the head coil. Fixation subtended 0.3° x 0.3° visual angle and stimuli subtended between

1.4° x 0.3° and 1.7° x 0.3° visual angle. All stimuli were presented in lower case. Responses were made with a button press, using either the index or middle finger of their right hand to indicate “yes” or “no.” The response fingers were counter-balanced across participants.

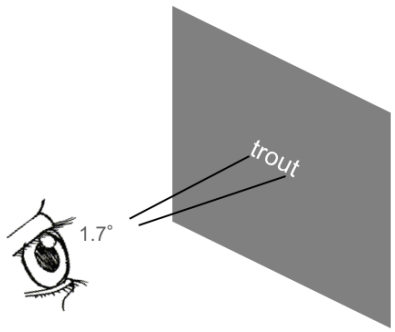



*Figure 26. Reading stimuli presentation. Stimuli were projected onto in-bore screen and had a width that subtended to maximum 1.7° visual angle*

Crucially, the same stimuli were used across the different tasks to ensure that task effects were due to processing differences rather than to changes in the stimuli. In other words, the word trials (HF & LF) were identical across tasks. The other stimuli were also held constant, but not all conditions were present in all tasks. This design allowed high-level task demands to be manipulated while controlling for differences in visual form.

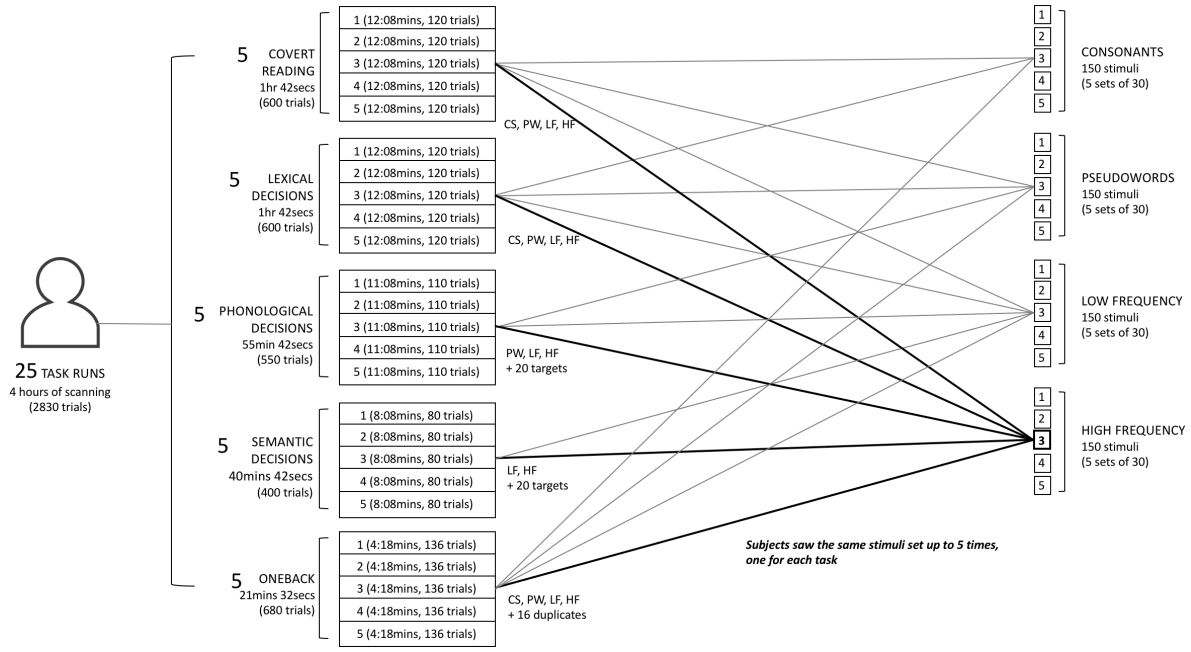



*Figure 27. Each participant performed 25 task runs for over 4 hours of scanning time. Participants saw the same stimuli lists up to 5 times, one for each task.*

## 2.12. Procedure

Each task was performed in separate runs and participants performed each task five times – once for each stimulus list. Thus, after the 25 runs, each stimulus had occurred in each task. Participants were given practice trials for each task inside the scanner before the experimental trials began. Stimuli that were used in the practice trials were not re-used in the experimental trials. All runs were carried out in mixed block and event related design. The four reading tasks (covert reading, lexical decisions, phonological decisions and semantic decisions) used very similar procedures. In contrast, the working-memory task used a different procedure.

| | | | STIMULI BLOCK | | | REST BLOCK | | |
|---|---|---|---|---|---|---|---|---|
| TASK | TRIALS (per run) | ISI (ms) | # | TRIALS | TIME (s) | # | TIME (s) | TIME (mm:ss) |
| Covert Reading | 120 | 2250-5500 | 12 | 10 | 45 | 12 | 16 | 12:08 |
| Lexical Decisions | 120 | 2250-5500 | 12 | 10 | 45 | 12 | 16 | 12:08 |
| Phonological Decisions | 110 | 2250-5500 | 11 | 10 | 45 | 11 | 16 | 11:08 |
| Semantic Decisions | 80 | 2250-5500 | 8 | 10 | 45 | 8 | 16 | 8:08 |
| One Back | 136 | 250 | 8 | 17 | 17 | 8 | 16 | 4:18 |

*Table 6. Stimuli presentation times by task.*

In the four reading tasks, blocks of task (45 seconds) were intermixed with blocks of fixation (16 seconds) in an A-B alternating design. For covert reading and lexical decision runs, blocks contained 10 trials with trials pseudo-randomly chosen from the four different stimulus categories. As a result, a run consisted of 12 blocks of stimuli, totaling 12:08 minutes of scanning. For phonological and semantic decision runs, on average, each block contained two target items and 8 stimuli chosen from the three or two stimuli conditions, respectively. As a result, phonological decisions had 11 blocks, totaling 11:08 minutes of scanning. Semantic decisions had 8 blocks, lasting 8:08 minutes. For all four of the reading tasks, individual trials began with a fixation cross presented for 500 msec before it was replaced by the stimulus for 250 msec. The screen then turned blank with a variable inter-stimulus interval ranging from 2250-5500msec for an average trial time of 4.5 sec.

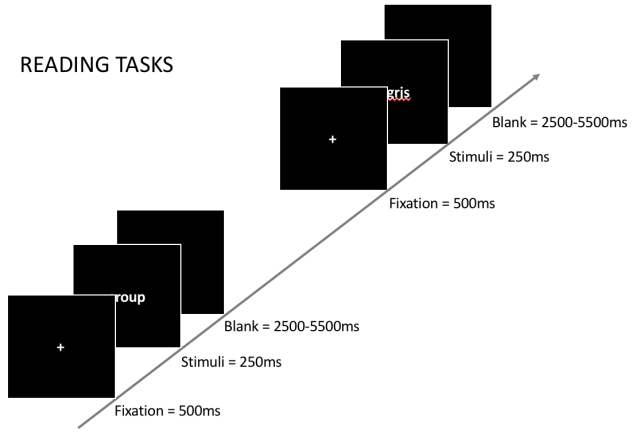



*Figure 28. Stimulus timing for the four reading tasks (covert reading, lexical decisions, phonological decisions, and semantic decisions).*

In the one-back task, blocks of task (17 seconds) were alternated with blocks of fixation (16 seconds) in an A-B design. Within a block, all the stimuli came from the same category (e.g. all HF words or all consonant letters strings) and were presented once a second for 250msec with a 250msec blank screen and a 500msec fixation cross separating trials. Each block had 17 trials composed of 15 stimuli and 2 targets (i.e. repeated items) and had a total run time of 4:18 minutes.

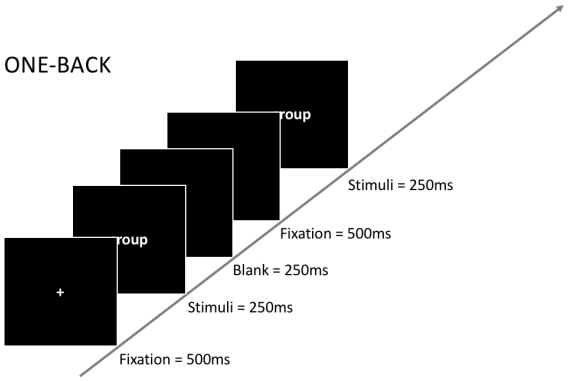



*Figure 29. Stimulus timing for the one-back task*

## 2.13. Scanning

Whole-brain imaging was performed on a Siemens 1.5T MRI scanner at the Birkbeck-UCL Centre for Neuroimaging (BUCNI). The functional data were acquired with the same gradient-echo EPI sequence used for visual field mapping (3.2 x 3.2 x 3.2mm, 24 slices, TR=2s, TE=39ms, 1474 MHz bandwidth) using the bottom half of a Siemens 32-channel head coil. The covert reading and lexical decision tasks runs consisted of 367 volumes and had a total run time of 12:08 minutes. The phonological decisions tasks consisted of 337 volumes and had a total run time of 11:08 minutes. The semantic decisions task consisted of 247 volumes and had a total run time of 8:08 minutes. The one-back task consisted of 128 volumes and had a total run time of 4:18 minutes. In addition, a single volume, full brain EPI scan (3.2 x 3.2 x 3.2mm) was acquired using the entire 32-channel head coil and the same slice prescription used in the reading tasks. This image increased the accuracy of the registration procedure for localizing the functional data on the participant's brain anatomy. The total acquisition time of reading and one-back data was approximately 4 hours per participant.

## 2.14. Image processing

Image processing was carried out using FSL 4.0 (www.fmrib.ox.ac.uk/fsl). To allow for T1 equilibrium, the initial two images of each run were discarded. The data were then realigned to remove small head movements (Jenkinson, Bannister, Brady, & Smith, 2002), smoothed with a 6-mm FWHM Gaussian kernel, and prewhitened to remove temporal autocorrelation (Woolrich, Ripley, Brady, & Smith, 2001). The pre-processed functional

volumes were analysed using a mass univariate general linear model approach. At the first level, stimuli onsets were convolved with a canonical haemodynamic response function (Glover, 1999). Temporal derivatives and estimated motion parameters were included as covariates-of-no-interest to reduce structured noise. A second level, fixed-effects model combined the five runs of the same task (e.g. lexical decision lists 1-5) into a single, participant-specific analysis. The results were then registered into the participant's high-resolution anatomical space so that they could be combined with the visual field masks for the visual area ROIs. This involved registering the first level partial-brain volume results to the participant's whole brain EPI scan, manually registering the whole-brain EPI to the structural scan, concatenating the registrations and applying them to the original data. So that the reading response data could be analysed per area, all the visual area ROIs were converted from surface space to 3D volume space using Freesurfer's *mri_label2vol* command. The results are presented in Chapters 3-5.

# *3. Top Down Effects of Reading in V1-V3*

## 3.1. Introduction

The two factors that most clearly distinguish the prominent neurological models of reading are i) the presence of top-down as well as bottom-up processing of visual information (i.e. directionality) and ii) the existence of reading-specific neuronal codes (i.e. specificity). According to Dehaene and colleagues' (2005) Local Combination Detector (LCD) model, visual information is processed in a serial, feedforward manner in early visual cortices until it arrives in ventral occipitotemporal cortex (vOT) where specialized neuronal populations encode orthographic information. In contrast, Price & Devlin's (2011) Interactive Account (IA) argues for a predictive coding model in which processing is always bi-directional, that is both bottom-up *and* top-down, and is never specialized for orthographic information. The specificity argument has received considerable attention (Cohen & Dehaene, 2004; Cohen et al., 2002; Glezer et al., 2009; Kronbichler et al., 2004; Price & Devlin, 2003, 2004) but of course, only applies to vOT and not to earlier visual areas. In contrast, the directionality argument explicitly applies to both vOT and to early visual cortices but has received relatively little attention. In this chapter I investigated bottom-up and top-down processing in V1-V3 during reading.

## 3.2. Top-down influences in vOT

The key principle of feed-forward accounts of early visual processing is that neuronal responses are driven almost entirely by the properties of a visual stimulus and not by extra-stimulus factors like the behavioural intentions of the organism. According to feed-forward

accounts of visual recognition, a hierarchical set of transformations aggregates the very basic information from retinal inputs into simple features in V1/V2 and then into a set of progressively more complex features encoded in the temporal lobes. A classic example would be Hubel & Wiesel's (1959) description of orientation-detectors in V1 of the anesthetized cat and their subsequent description (Hubel & Wiesel, 1962) of the complex cells in V2 that responded to a broader range of oriented stimuli. Tanaka (1993) extended these findings and demonstrated still more complex visual receptive fields in inferotemporal neurons along the ventral visual pathway. Visual recognition, according to these classical feedforward accounts, is driven in a bottom-up manner with visual receptive field responses being entirely determined by the specific spatial properties of the visual stimuli.

According to the LCD model (Dehaene et al., 2005), the vOT is the point in the visual hierarchy where bigram detectors combine information from letter detectors located in V4 and in turn project to morpheme or whole word detectors in more anterior parts of inferotemporal cortex. By this account, the critical factor for information processing in vOT is the presence of orthotactically legal letter combinations rather than how they are used. Factors like the specific task demands or word-level properties of the stimulus should be irrelevant. Studies have, however, repeatedly shown that these factors significantly influence processing in vOT suggesting that top-down influences may also play an important role during visual word recognition.

For example, Yang and Zevin (2014) had participants perform two different tasks on the same set of stimuli. One was a standard visual lexical decision task while the other was a symbol detection task in which participants responded when they saw an infrequent symbol

(%) in the stimulus. The authors reported a main effect of Task with lexical decision producing significantly greater activation in vOT than symbol detection, despite the presence of identical stimuli. One could argue that lexical decision was simply a more difficult task than symbol detections – and indeed, the RTs were longer – and thus an increase in vOT signal simply reflected increased attentional demands. In other words, the basic computation being performed in vOT was not changing as a result of top-down influences; instead vOT just had to work harder in one task than the other. To address this concern would require not just a quantitative shift in vOT responses but a different qualitative pattern.

Hellyer and colleagues (2011) demonstrated that task demands can influence more than just the strength of vOT activity. In their experiment, subjects viewed numbers written as numbers (e.g. "22") or as words (e.g. "twenty-two") and had to make a decision based either on the numeric value (e.g. is the number even or odd?) or on its sound (e.g. "does it contain an 'n' sound?"). For numeric decisions, only numbers written as words significantly engaged vOT. In contrast, for phonological decisions, both numeric and word-based numbers activated vOT equally. In other words, changing the task requirements did more than change the magnitude of the response, there was a qualitative shift in vOT activity.

Many studies have demonstrated that manipulating stimulus properties can also affect processing in vOT, even when low-level factors like bigram frequency are held constant. For instance, Fiebach et al. (2005) showed the repetition of real words had a very different effect on activation in vOT than repeating pseudowords. Specifically, presenting a word in quick succession (e.g. "bird…bird") led to repetition suppression in vOT while repeating

pseudowords (e.g. “pund…pund”) enhanced vOT activation (see also Devlin et al., 2006) In both cases, the exact same bigrams were present in the prime and target but the pattern of results depended on a factor not present in the visual stimulus, namely the lexical status (e.g. word or nonword) of the letter string. Twomey et al. (2011) reported a similar modulation of vOT responses in a lexical decision task in which participants saw real words (e.g. “stone”) and pseudohomophones (e.g. “stoan”) – that is nonwords that sound like real words. They were asked to decide whether each stimulus was a genuine English word or not based on its orthography. Within vOT, pseudohomophones elicited significantly greater activation than English words despite matching the stimuli for bigram frequency and other low level visual and orthographic properties. In both examples, the authors interpreted their findings as clear evidence of top-down modulation of neuronal responses in vOT.

Additional evidence for top-down modulation of vOT during reading comes from experimental studies using methods with better temporal resolution than fMRI. For example, several MEG studies have reported word-related activity in Broca’s area during reading as early as 130 milliseconds (ms) post-stimulus onset (Cornelissen et al., 2009; Pammer et al., 2004; Wheat et al., 2010). Woodhead and colleagues (2014) investigated its role using a combination of MEG and dynamic causal modelling (David et al., 2006). They found top-down modulation from Broca’s area to vOT that was stronger for real words than nonwords. A similar experiment by Chen and colleagues (2015) used combined EEG/MEG and found that both word frequency and imageability systematically affected processing in vOT at 160 milliseconds post stimulus onset, suggesting that vOT integrates perceptual input (i.e. bottom-up processing) with prior knowledge (i.e. top-down processing). Finally, a chronometric TMS study found that virtual lesions to vOT were most effective between 80-

200msec post stimulus onset – a much longer time window than expected for a feedforward pass through extrastriate cortex (Duncan, Pattamadilok, & Devlin, 2010). The authors interpret the prolonged window of vulnerability as indicative of interactions between vOT and the supramarginal gyrus, another region important for visual word recognition (Sliwinska, James, & Devlin, 2015).

A final line of evidence suggesting that processing in vOT is not strictly feedforward comes from studies showing lexical frequency effects in vOT (Chee, Lee, Soon, Westphal, & Venkatraman, 2003; Graves, Desai, Humphries, Seidenberg, & Binder, 2010; Hauk, Davis, Kherif, & Pulvermüller, 2008; Hauk, Shtyrov, & Pulvermüller, 2008; Kronbichler et al., 2004). In terms of behaviour, the number of times a person has encountered a word is an important factor in how quickly s/he recognises that word (Balota et al., 2004; Balota et al., 2006). In the brain, word frequency effects have been found in various frontal, temporal, parietal, and occipital regions. In vOT, Kronbichler et al. (2004) found that activation was inversely correlated with whole-word lexical frequency. That is, common words such as "book" produced less activation than less common words like "beaver." Moreover, pronounceable letter strings that follow orthotactic constraints (pseudowords) such as "bram" produced the most activation in vOT. These findings are inconsistent with the LCD model because word frequency is not a property of bigrams but of entire words. By ensuring that bigram frequency was carefully matched across their word frequency bands, Kronbichler et al. (2004) could rule out any explanation that relied on stimulus-bound bigram detectors in vOT. Instead, the authors' suggested that neurons in vOT were whole-word detectors sensitive to frequency – essentially a neuronal analogy to Morton's (1969) logogens. Although this explanation suffices to explain some findings (e.g. their own and

Glezer et al., 2009), whole word detectors fail to account for the other top-down effects listed above and a range of other basic stimulus effects (see Devlin et al., 2006; Starrfelt & Gerlach, 2007 for a full explanation). The interactive account (Price & Devlin, 2011), however, can easily explain word frequency effects in vOT in terms of the top-down integration of prior knowledge.

In summary, there is considerable evidence suggesting that, at least as early as vOT, visual word recognition involves both top-down influences and stimulus-driven (uncontroversial), bottom-up processing. The directionality argument is not limited to vOT, however, and applies to the early visual cortices as well.

### 3.3. Top-down influences in early visual cortices

Serial feedforward accounts of early visual processing are inconsistent with a growing body of evidence suggesting that processing, even in the earliest visual areas, is better characterised as interactive, feedback rich, and subject to cortico-cortico influence from higher-order regions (Kravitz et al., 2013). Anatomically, feedback connections predominate in much of the primate visual system (Salin & Bullier, 1995). Indeed, V1 neurons receive far more input from V2 alone than it receives from the retinogeniculate pathway (Budd, 1998; Peters et al., 1994). Furthermore, there is mounting evidence that extra-classical input into V1 neurons includes projections from more distal circuits and even different sensory systems. In monkeys for example, the auditory cortices send monosynaptic projections to V1 (Falchier et al., 2002; Rockland & Ojima, 2003). These auditory projections are

particularly dense to V1 regions representing the periphery of the visual field (Falchier et al., 2002; Rockland & Ojima, 2003). Preliminary evidence from diffusion-weighted tensor imaging (Beer et al., 2011) suggests that there are similar connections in humans. How such diverse feedback contributes to early visual processing is not well understood.

Top-down factors like behavioural intentions can dramatically alter how early visual areas respond to stimulation. For example, the exact same visual stimuli are processed differently (as measured by BOLD response) depending on whether the subject is preparing to make a decision based on their physical (e.g., colour) or conceptual (e.g., man-made) properties (Harel, Kravitz, & Baker, 2014). Further, as mental imagery studies demonstrate, non-retinal sources are capable of activating striate and extrastriate cortices without any visual stimulation at all (see Kosslyn & Thompson, 2003 for a review). Moreover, when retinotopic mapping procedures are used, mental imagery driven responses are remarkably consistent with the topographic pattern of activity produced during actual perception (Slotnick, Thompson, & Kosslyn, 2005).

The integration of audio-visual signals, according to evidence from more temporally sensitive measurements, happens early. Multimodal investigations using TMS (Romei, Murray, Cappe, & Thut, 2009) and EEG (Campus, Sandini, Concetta Morrone, & Gori, 2017) both show that auditory input facilitates V1 response around 50-80ms. Crucially, auditory influence on V1 activity depends on the nature of the stimuli and demands of the task. TMS-based measurement of low-level visual cortex excitability (i.e., phosphene induction) show that 'looming' structured auditory sounds, thought to be more behaviourally salient, produce greater V1 facilitation than other sound categories and white-noise controls (Romei

et al., 2009). Further, EEG measurements show that auditory stimulation has almost no effect during a temporal localization task but produces a 10-fold increase in an early occipital event-related potential when presented in a spatial localization task (Campus et al., 2017). Early and task dependent audio-visual interactions is also consistent with electrophysiological evidence in monkeys. For example, it takes less time for V1 to respond during multisensory (~60ms) than visual (~65ms) trials but only during an active, but not passive, behavioral task (Wang, Celebrini, Trotter, & Barone, 2008). How exactly these early multimodal influences facilitate early visual processing is still not clear but they do raise the possibility, although speculative, that the early visual cortices receive phonological feedback from perisylvian neural circuits involved in reading.

Activity patterns in V1/V2 do appear to contain enough information to discriminate different sound categories (bird singing, traffic noise, and a talking crowd). Using fMRI combined with multivariate pattern analysis (MVPA), Vetter and colleagues (2014) could successfully identify the category of auditory stimulation based only on the activity pattern in retinotopically defined V1/V2. Crucially, however, classification was only successful in peripheral and far peripheral areas and not in foveal regions (Vetter et al., 2014). One possibility, the researchers suggested, is that auditory circuits transmit sensory predictions to V1 in the same (but cross-modal) way that higher visual areas are thought to project predictions back to V1, for example during motion perception (Muckli et al., 2005; Vetter, Grosbras, & Muckli, 2015).

## 3.4. Specific questions

My aim in this chapter is to determine whether the early visual cortices contribute more to reading than just the feedforward extraction of basic spatial features. To do this, I first examined the activation maps for reading within each of the early visual areas to determine whether activation is essentially restricted to the horizontal meridian (where the written stimuli were) or whether it extends to other less central areas as well. Next, I looked for effects of the different reading tasks on activation within early visual areas to determine whether task significantly affects processing in these areas as it has been shown to in vOT (Hellyer et al., 2011; Mano et al., 2013; Yang & Zevin, 2014). Finally, I looked to see whether the different stimuli conditions affected processing in early visual regions. Specifically, I examined whether lexical frequency had any influence on the activations. Evidence of task or word frequency effects in the early visual cortices (V1-V3) would provide strong evidence that reading involved not only feedforward visual processing, but also top-down contributions as well.

## 3.5. Methods

The data in this chapter come from the four reading experiments (i.e. covert reading, lexical decisions, phonological decisions, semantic decision) but not the one-back task, which is reported separately in Chapter 5.

The behavioural data were analysed for accuracy, response time and sensitivity. Response time (RT) analyses were conducted for the lexical decisions task, which was the only task requiring a response for each trial. A one-way ANOVA with Stimuli (consonant string,

pseudowords, low frequency words & high frequency words) as independent factors evaluated the main effect of stimulus type. A planned comparison also compared RTs between low and high frequency words. Finally, because phonological and semantic decisions involved only occasional responses, a sensitivity score (d') was computed. By definition covert reading produced no overt responses to analyze.

A full description of the image analyses used here can be found in the previous chapter. In brief, ROIs for visual areas V1, V2, and V3 were defined retinotopically in each hemisphere. A forth ROI, vOT, was included because previous reading investigations have identified task and stimulus effects in this region. As a result, it was important to include vOT in order to determine whether these previous findings replicate. vOT was defined using the standard space coordinates: x= ±30 to ±54, y= ±45 to ±70 and z= ±30 to ±4 as per Twomey et al. (2011). This definition encompassed the posterior portion of the fusiform gyrus, occipito-temporal sulcus, and medial parts of the inferior temporal gyrus bilaterally: areas consistently activated by visual word recognition tasks. The coordinates also included parts of the cerebellum, but these were removed to limit the region to ventral occipito-temporal cortex.

The first statistical analysis investigated whether high-level task requirements influenced neural activity in the early visual areas using a 2 × 4 × 4 ANOVA with Hemisphere (left, right), Task (lexical decisions, semantic decisions, phonological decisions, and covert reading), and Area (V1, V2, V3, and vOT) as independent factors. The dependent measure was mean effect size calculated as the percent BOLD signal change from the voxels 'activated' by the contrast of the four stimuli categories relative to rest. Activation was determined using a

voxel-wise threshold of Z>2.3 (or p<0.01 uncorrected for multiple comparisons). Note that a range of statistical thresholds (Z>1.96, Z>2.3, and Z>3.1) all yielded essentially similar results across all of the analyses reported in this chapter so the specific threshold (Z>2.3) was an arbitrary choice.

The second analysis investigated whether the type of stimuli influenced neural activity in early visual areas using a similar 2 × 4 × 4 ANOVA. In this case, the independent factor Task was replaced with Stimuli (consonant letters, pseudowords, low frequency words, and high frequency words) but otherwise it was identical to the previous analysis.

A final analysis investigated how the central (stimulated) foveal/parafoveal region of V1-V3 responded to the different task and stimuli manipulations.

## 3.6. Results

### 3.6.1. Behaviour

In the three tasks requiring responses (i.e. lexical decisions, phonological decisions, and semantic decisions), accuracy was very high (m=94%) and did not differ significantly between the tasks ($F(2,6)=3.29$, $p=0.11$; see Figure 30A). For the lexical decisions task, the only task requiring a response for each trial, I also analysed response time. Responses were fastest to consonant strings (703ms), followed by high frequency (744ms), and then low frequency words (815ms), with responses being slowest for pseudowords (933ms). A one-way repeated measures ANOVA confirmed a highly significant difference between conditions [$F(3,9)=22.2$, $p<0.001$] and a subsequent one-tailed t-test confirmed a significant

advantage for high relative to low frequency words (t(3)=3.3, p=0.022) (see Figure 30B). As the phonological and semantic decisions involved only occasional responses, a sensitivity score (d') was computed. Sensitivity did not significantly differ between the two tasks [t(3)=-1.57,p=0.22].

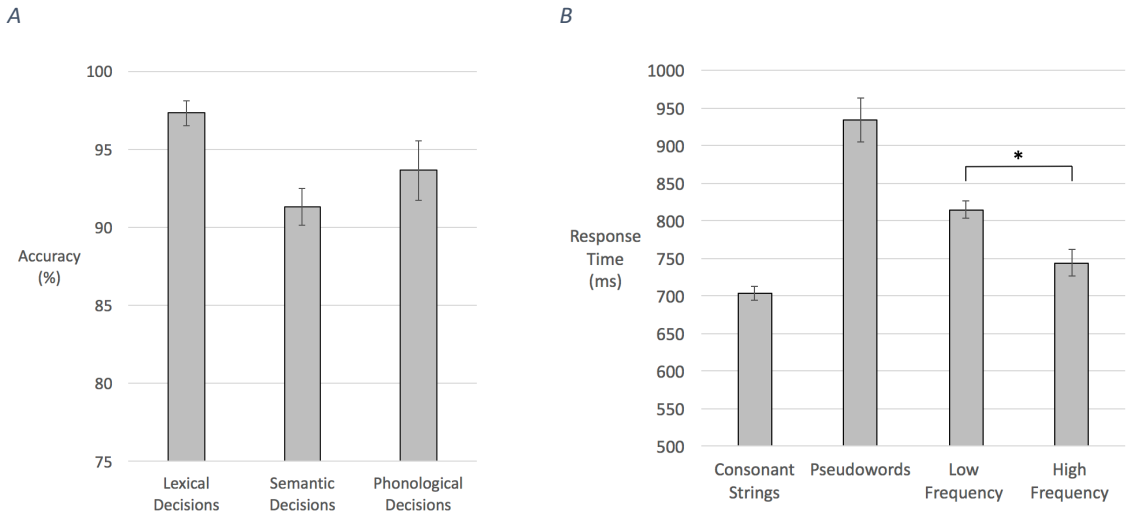
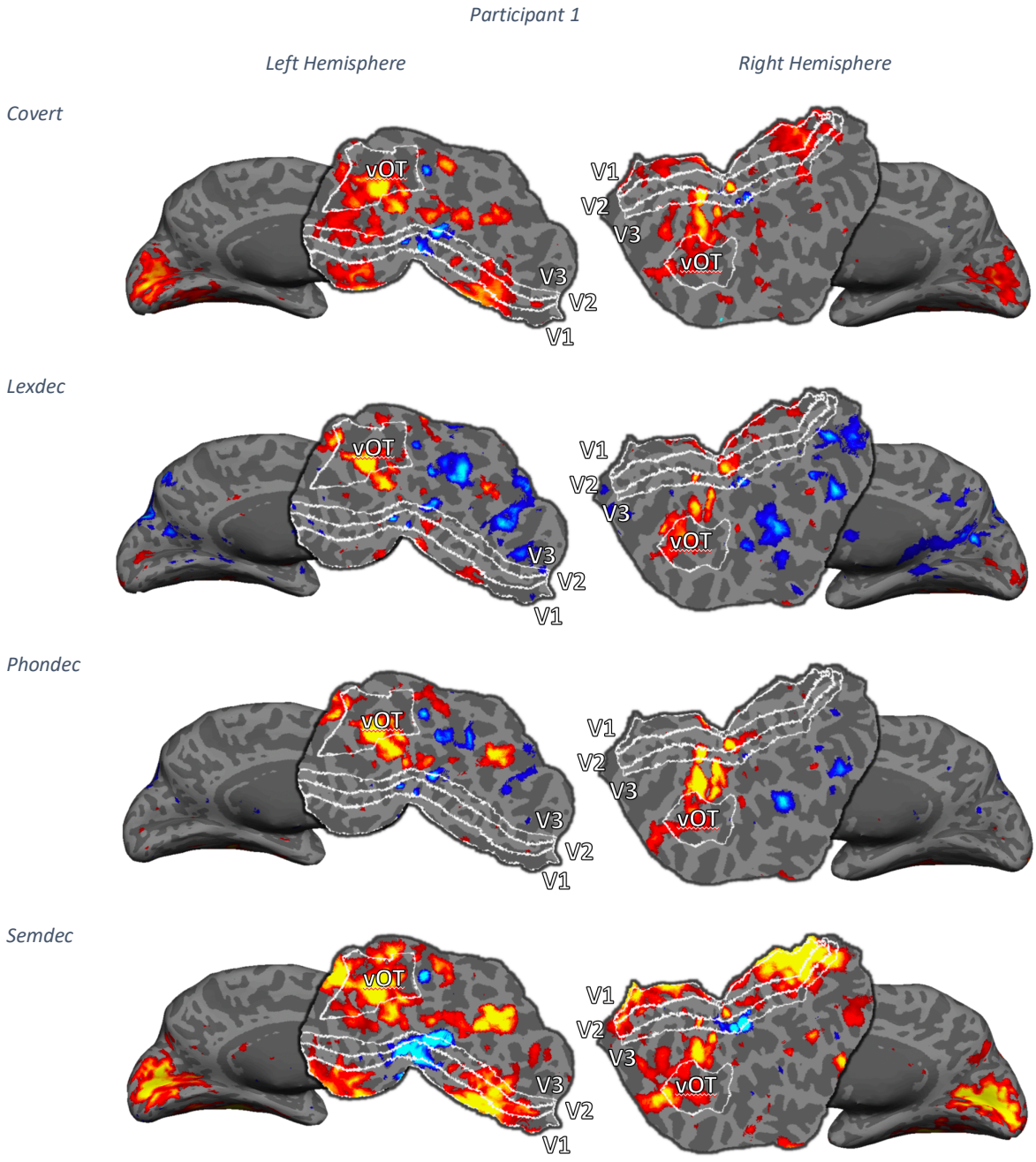



*Figure 30. (A) Response accuracy by task. Average accuracy across the three tasks was high (m=94%) indicating that the participants were highly engaged while in the scanner. (B) Response times in the lexical decisions task. Participants were significantly faster at responding to high frequency words than to low frequency words. Error bars represent the standard error of the mean adjusted to correctly reflect within-subject error (Loftus & Masson, 1994) and the asterisk denotes a significant difference.*

### 3.6.2. BOLD response

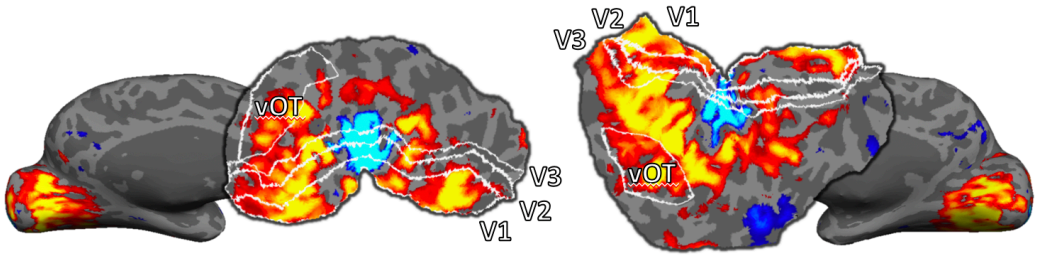
As anticipated, each of the reading tasks engaged the early visual areas (V1-V3) as well as vOT. Figure 31 shows one participant's pattern of activation (red-yellow) and de-activation (blue-light blue) in each of the four reading tasks. White lines delineate the borders between early visual fields while the white ovoid shape delineates vOT. Activation is clearly present in both the left and right hemispheres for all four regions-of-interest. Within bilateral V1-V3, there was activation in central foveal/parafoveal regions where the stimuli would have appeared. Activation was also not limited only to the central, stimulated regions

but was also present in more eccentric areas (>3.8 °) well outside the expected stimulated region (stimuli were shown at the point of fixation and had a maximum width subtending on 1.7° visual angle, see General Methods for more information). This basic pattern of activation was largely conserved across tasks with differences primarily in the magnitude and spatial extent of the activations but not their spatial pattern.



*Participant 2*

*Covert*

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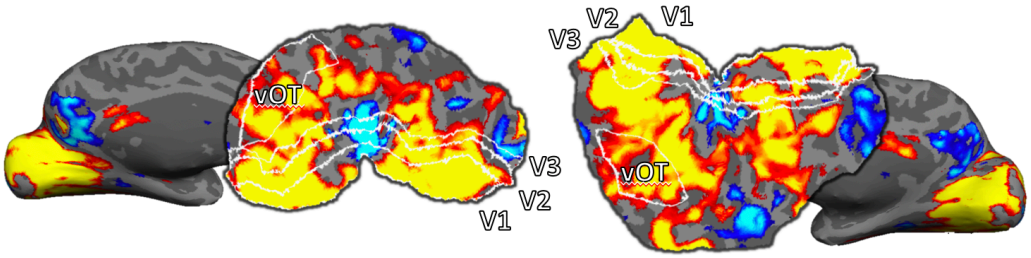


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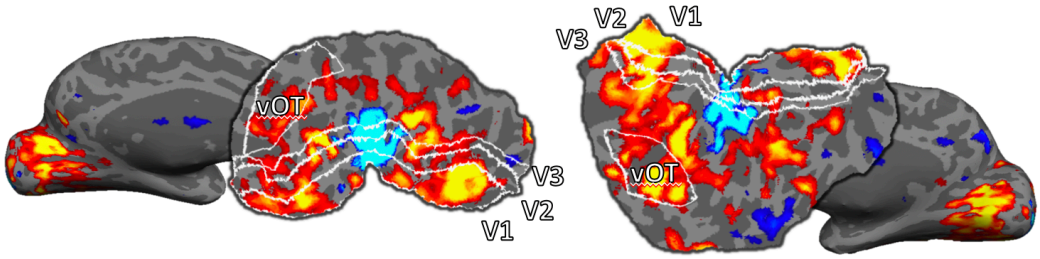


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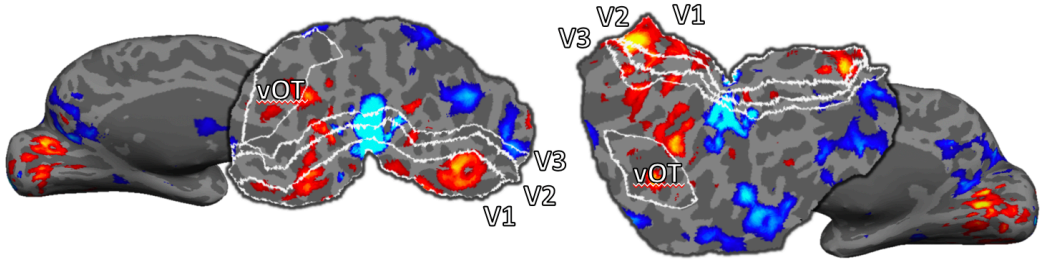


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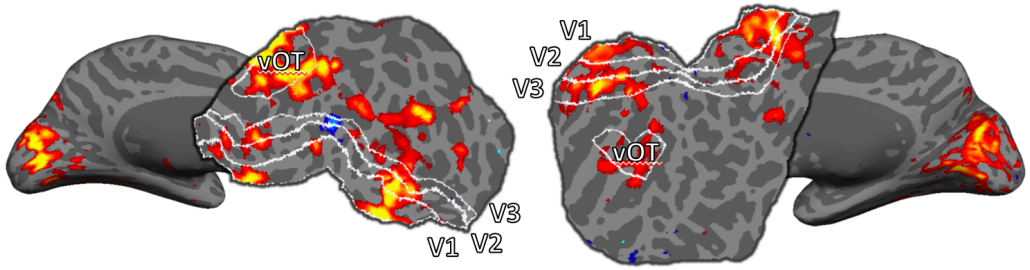
*Covert*



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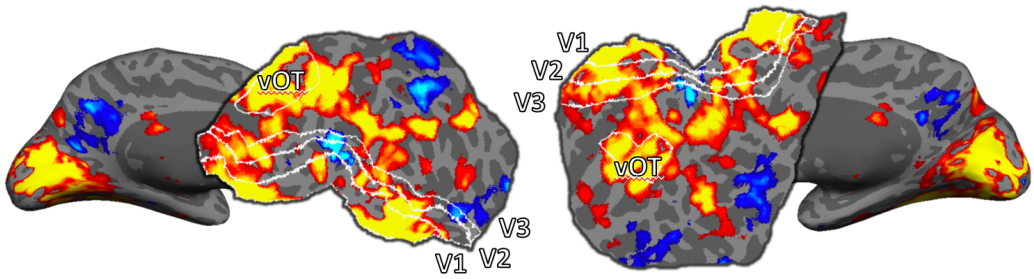


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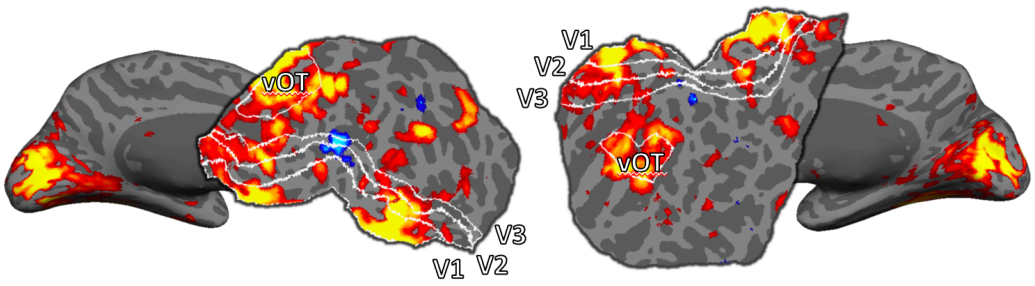


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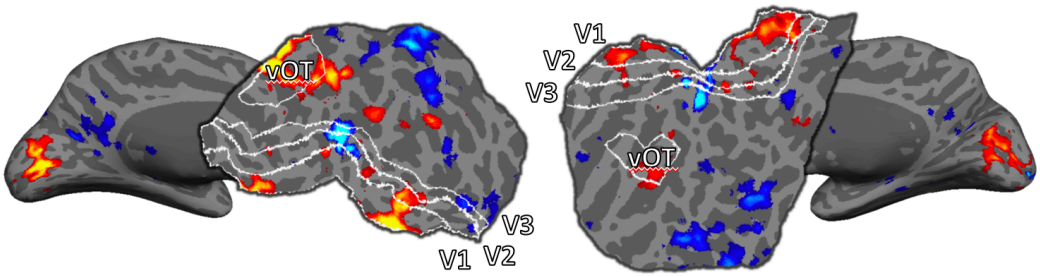
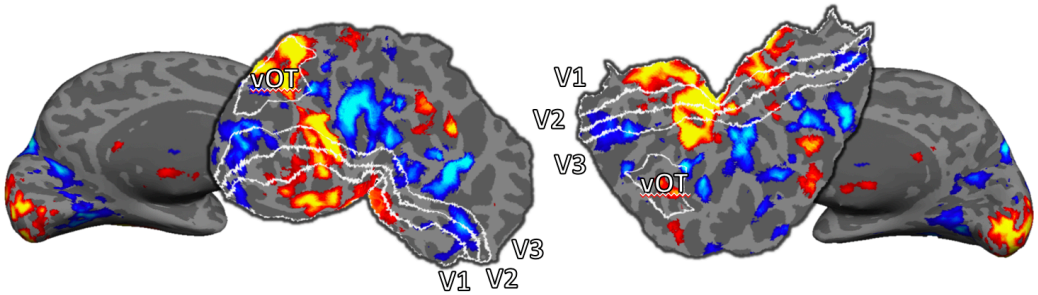



*Participant 4*

*Covert*

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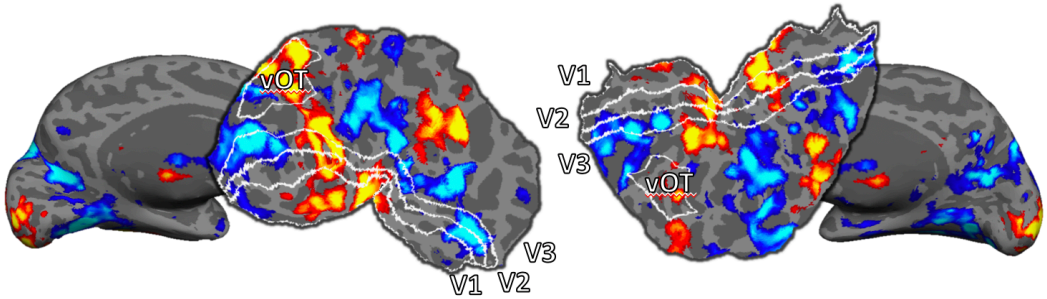


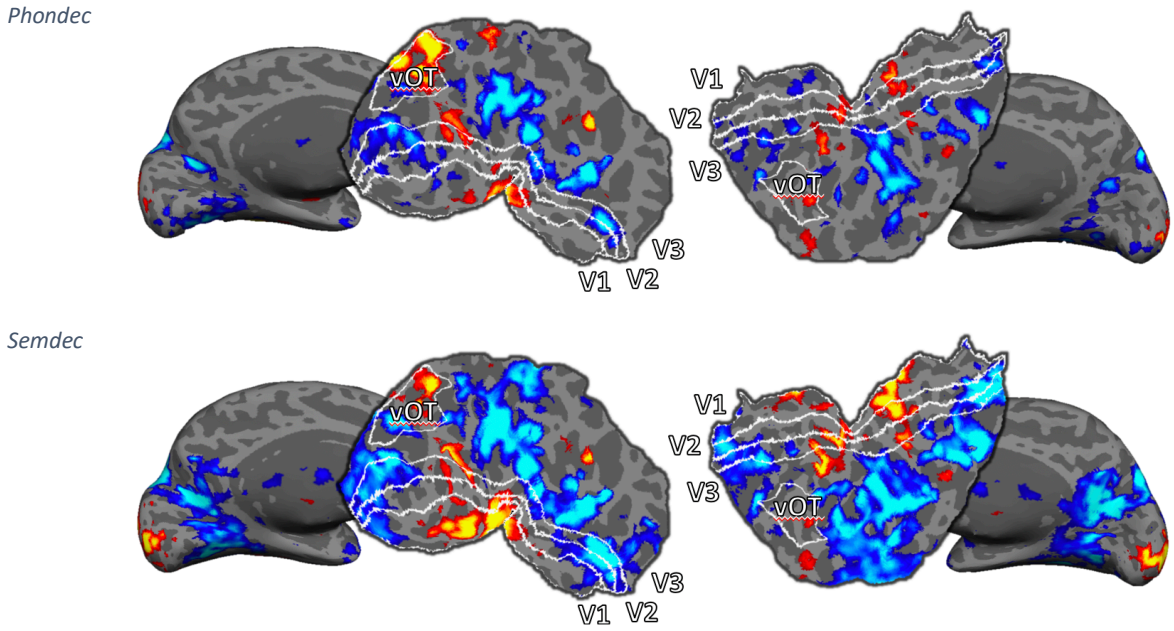



*Figure 31. All four participant's brain activation during the four different reading tasks (words > rest) shown on the inflated (background) and flattened surfaces of left and right hemispheres. Activations are thresholded at Z>2.3. As can be seen, reading engaged areas V1-V3 and vOT cortices bilaterally. Area borders a shown in white. The light and dark gray colouring represent gyral and sulcal regions respectively.*

To investigate whether high-level task requirements influenced neural activity in the early visual areas, a 2 × 4 × 4 ANOVA with Hemisphere (left, right), Task (lexical decisions, semantic decisions, phonological decisions, and covert reading), and Area (V1, V2, V3, and vOT) as factors. This analysis revealed a main effect of Area [$F(3,9)=3.925$, $p=0.048$] with V1 showing the largest BOLD signal changes. Moving up the visual hierarchy, the strength of response diminished from V1 to vOT (see Figure 32A). Post-hoc t-tests confirmed that activation in V1 was significantly greater than in V3 ($t(3)=5.326$, $p=0.013$). No other comparisons were significant after Bonferoni correction (all $p>0.11$). The main effects of Hemisphere ([$F(1,3)=0.010$, $p=0.926$]) and Task ([$F(3,9)=2.042$, $p=0.179$]) were not significant.

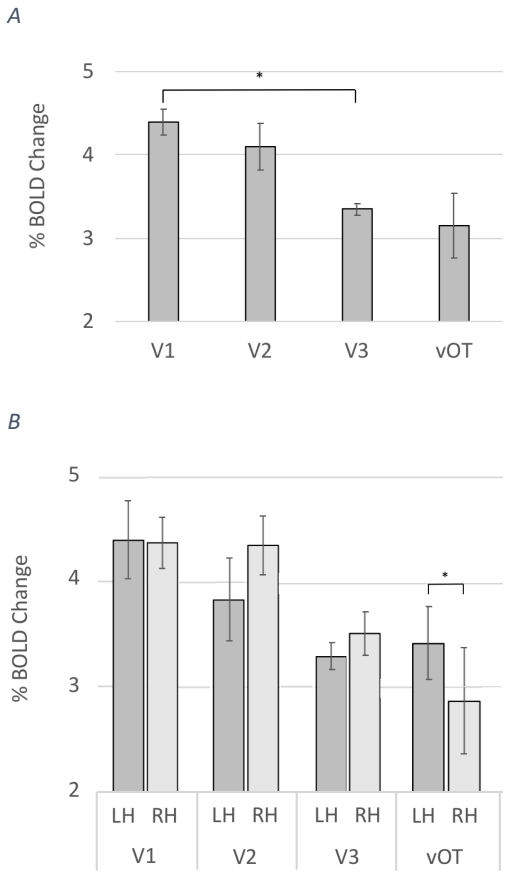



*Figure 32. Reading effect size by area. (A) Area effect size, shown as % BOLD signal change, collapsed over the four tasks and conditions (LF > rest, HF > rest, PW > rest, and CS > rest). Activation was greatest in V1, significantly greater than V3, and decreased moving up the visual hierarchy. (B) Effect size from (A) broken out by hemisphere. In the left hemisphere (B) effect size in the vOT is greater than in V3, breaking the trend seen in the right hemisphere and cross-hemisphere averages (A). As indicated by the asterisk, effect size was significantly greater in the left than right vOT.*

There was a Hemisphere × Area interaction [$F(3,9)=6.984$, $p=0.010$] indicating that, between areas V1 and vOT, an asymmetry emerges where reading is processed differently in one hemisphere than in the other. As can be seen in Figure 32B, in the left hemisphere the effect size is greater in vOT than in V3, reversing the general pattern of decreasing activation from V1-to-vOT found in both the right hemisphere (see Figure 32C) and the average across the two hemispheres (see Figure 32A). Activation in left vOT was significantly greater than in the right ($t(3)=19.7$, $p<0.01$). None of the others showed a significant difference in activation between the hemispheres (all $p>0.2$ after Bonferoni correction).

Lastly, the Task × Area interaction was also significant [$F(3,9)=2.694$, $p=0.022$] indicating that the involvement of the four different areas in reading depends on the reading task being

performed. To investigate this interaction further, for each of the four regions I ran a 1 × 4 one-way ANOVA with Task as the independent factor. None of the regions showed a significant main effect of Task, although there was a trend for vOT [F(3,9)=2.768, p=0.103]. Within vOT, activation during lexical decisions was significantly greater than during phonological decisions (t(3)=3.604, p=0.037) and nearly-significantly greater than during semantic decisions (t(3)=2.413, p=0.095). All other comparisons had a p<0.228. In other words, although there was a significant Task × Area interaction, the effect was subtle and appeared to be driven by vOT rather than the early visual cortices.

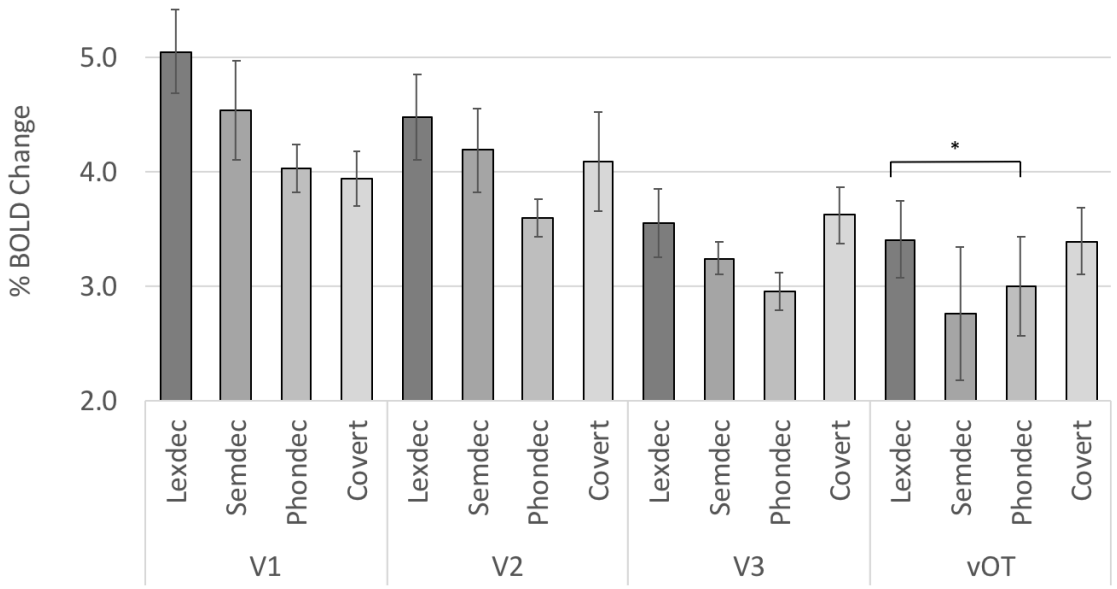



*Figure 33. Area effect sizes for each of the four tasks (collapsed over condition). In the vOT, the lexical decisions task had a significantly greater response than the phonological decisions task indicating that task requirements are a factor in processing within the region. Error bars represent the standard error of the mean.*

Neither the Hemisphere × Task [F(3,9)=1.960, p=0.191] nor the 3-way interaction [F(9,27)=0.830, p=0.595] were significant. In other words, like previous studies (Hellyer et al., 2011; Mano et al., 2013; Yang & Zevin, 2014) I observed task effects in vOT, but there was no evidence that Task significantly influenced processing in early visual fields (V1-V3).

A second analysis evaluated whether stimuli conditions influenced activity in the early visual areas. A 2 × 4 × 4 repeated measures ANOVA with Hemisphere (left, right), Area (V1, V2, V3, and vOT), and Stimuli (low frequency words, high frequency words, pseudowords, and consonant strings) as factors. As expected from the previous analysis, there was a main effect of Area F(3,9)=4.074, p=0.044] and a significant interaction of Hemisphere × Area F(3,9)=7.109, p=0.010]. Further, there was a significant Area × Stimuli interaction [F(3,9)=4.155, p=0.002] indicating that not all areas respond equivalently to the different stimuli types. To investigate this interaction further, four separate 1 × 4 ANOVAs with Stimuli as the independent factor were computed for each of the four areas. There was a main effect of Condition in vOT [F(3,9)=5.068, p=0.025] but not in V1 [F(3,9)=2.609, p=0.116], V2 [F(3,9)=0.351, p=0.790], or V3 [F(3,9)=1.531, p=0.304]. Because frequency has previously been shown to influence processing in vOT (Chee, Westphal, Goh, Graham, & Song, 2003; Kronbichler et al., 2004), I conducted a planned comparison of high vs. low frequency words in vOT and replicated the finding of greater activation for low relative to high frequency words (t(3)=2.512, p=0.048). In summary, there was no evidence that stimuli effects drove differences in early visual cortices; the only differences were observed in vOT and were at least partially due to a significant lexical frequency effect.

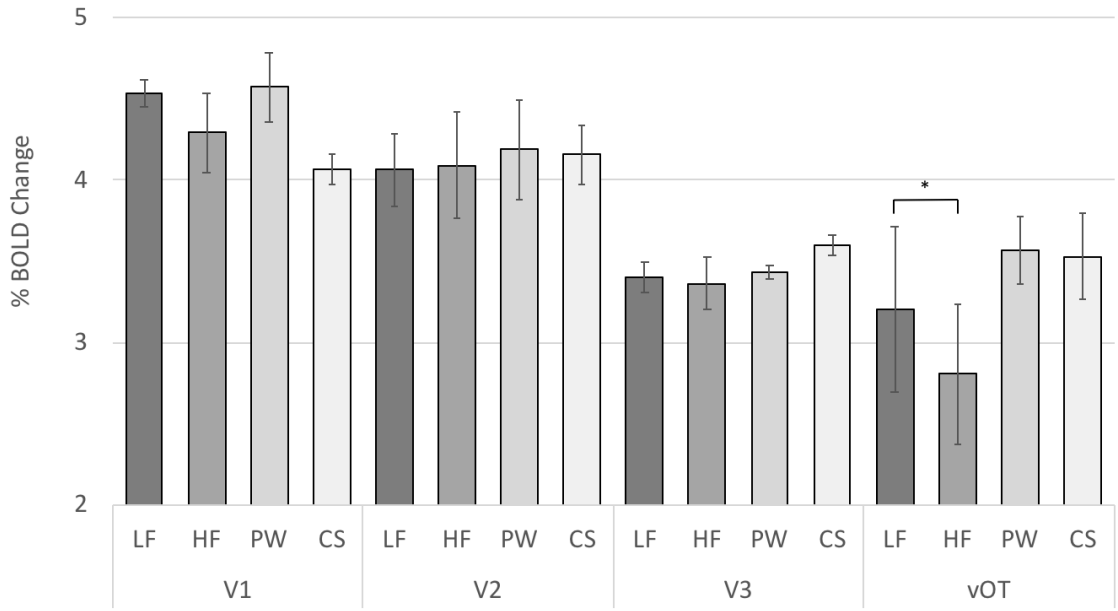
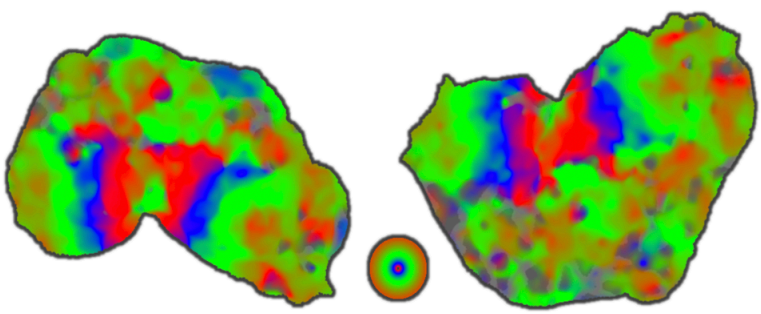



*Figure 34. Effect size for each condition by area, collapsed over task and hemisphere. Condition effect sizes were only compared in the vOT and only for Low Frequency words and High Frequency (HF) words. This comparison was planned in advance because frequency has previously been shown to influence processing in vOT (Chee, Westphal, et al., 2003; Kronbichler et al., 2004). The asterisk denotes a significant difference and error bars represent the standard error of the mean.*

It is possible to probe this issue in greater detail, though, especially given that activation in early visual areas was not limited to the central region along the horizontal meridian but also consistently included large areas of the periphery (>3.8° visual angle), far outside of the directly stimulated region (see Figure 35).

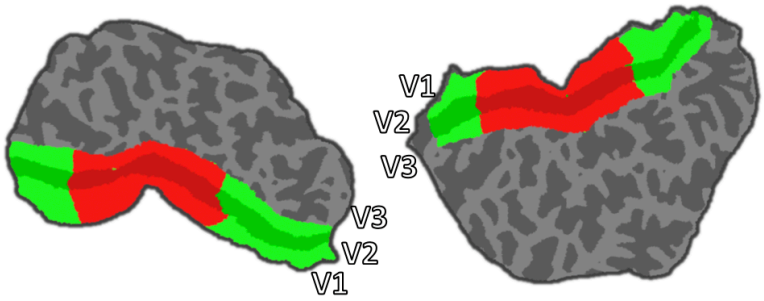
*Participant 1*

*A – Eccentricity retinotopic map*

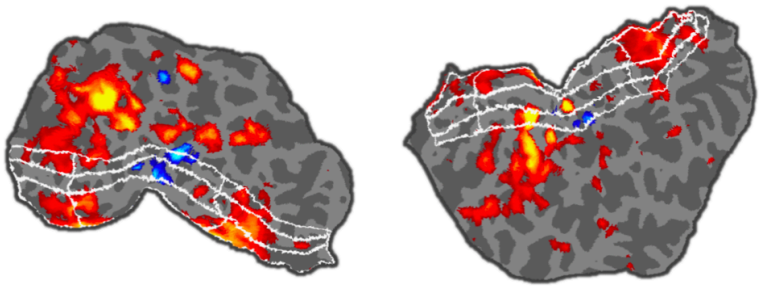


*B – Central (red) and Peripheral (green) regions of interest*

*Figure 35. Central and peripheral activation during reading. (A) Participant's retinotopic map of eccentricity shown on their flattened left and right hemisphere occipital patches. (B) The participant's central (red) and peripheral (green) ROIs encompassing cortex mapped to <= 3.8° and >3.8° in the visual field (maximum stimuli width subtended 1.7°). (C) the participant's brain activation during the covert reading task (words > rest). Activations are thresholded at Z>2.3*

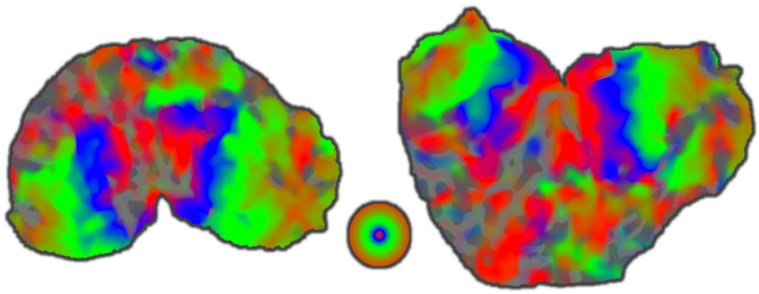



*C – Brain activation during covert reading task (words > rest)*

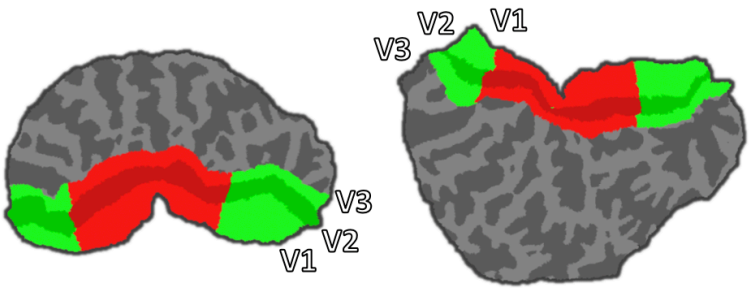


*Participant 2*

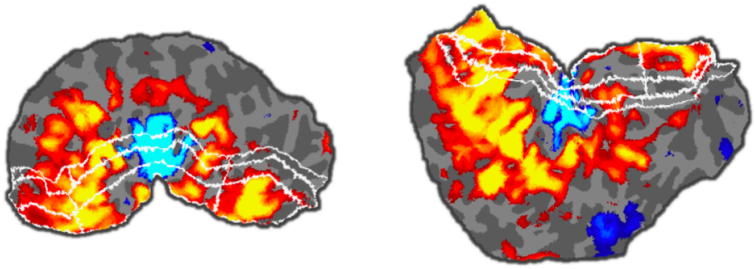
*A – Eccentricity retinotopic map*



*B – Central (red) and Peripheral (green) regions of interest*

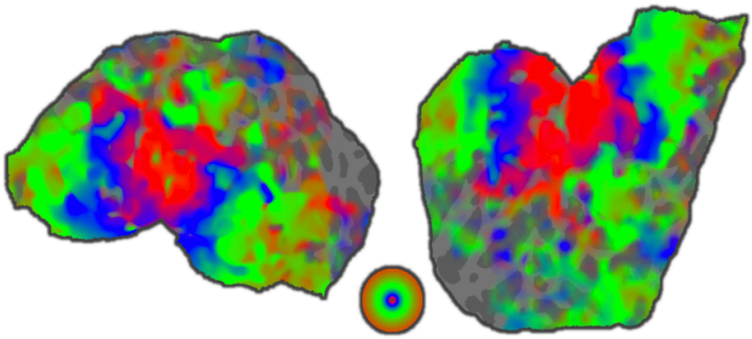



*C – Brain activation during covert reading task (words > rest)*

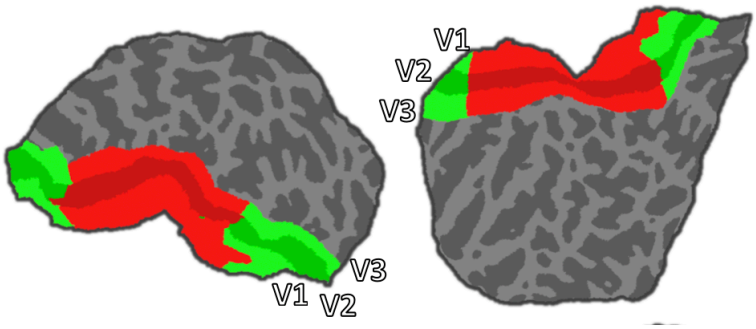


*Participant 3*

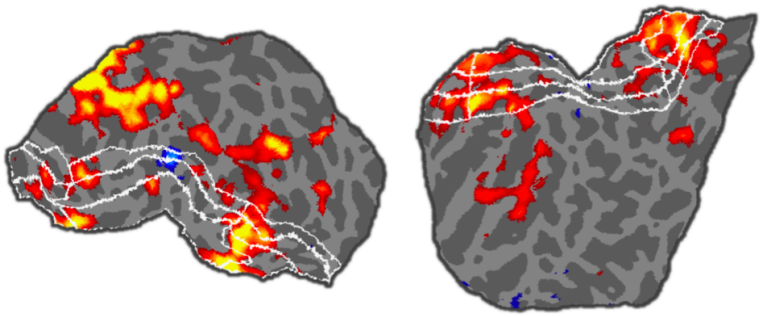
*A – Eccentricity retinotopic map*



*B – Central (red) and Peripheral (green) regions of interest*

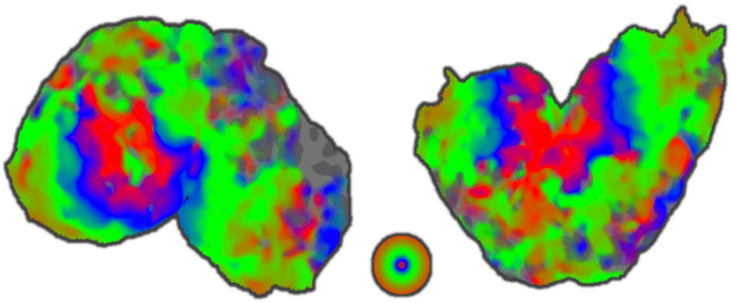



*C – Brain activation during covert reading task (words > rest)*

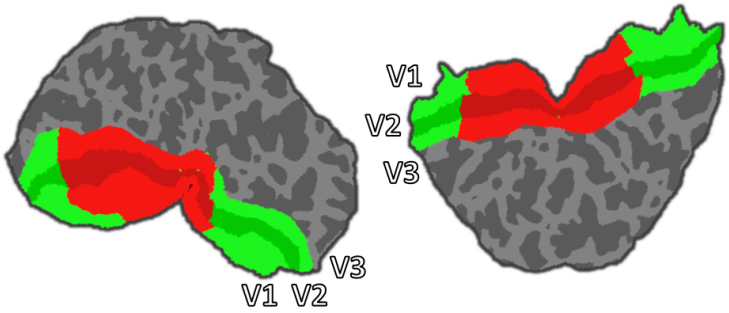


*Participant 4*

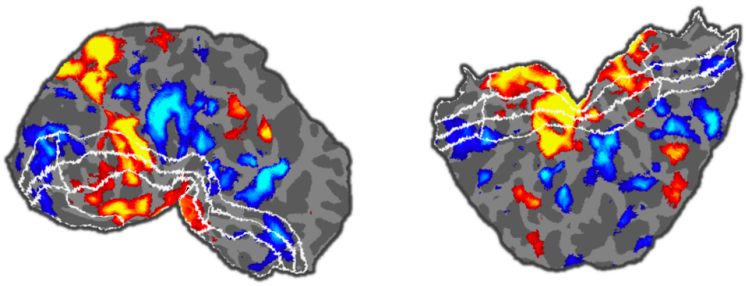
*A – Eccentricity retinotopic map*



*B – Central (red) and Peripheral (green) regions of interest*




*C – Brain activation during covert reading task (words > rest)*



Consequently, I ran a second analysis that only included V1-V3 activation found within the central, stimulated region, between 0° to 3.8°. Because vOT does not have a clear retinotopic organization, the region was excluded from this analysis resulting in a 2 (Hemisphere) × 4 (Stimuli type) × 3 (Area: V1-V3) ANOVA with BOLD signal change in the

central region the dependent measure. A significant main effect of Area [F(2,6)=4.076, p=0.076] confirmed decreasing activation from V1 (1.6%) to V2 (0.8%) to V3 (0.1%), as reported above (see Figure 36). There were no main effects of Hemi F(1,3)=1.380, p=0.325] or Stimuli Type [F(2,6)=0.502, p=0.690] and no significant interactions [all p>0.263].

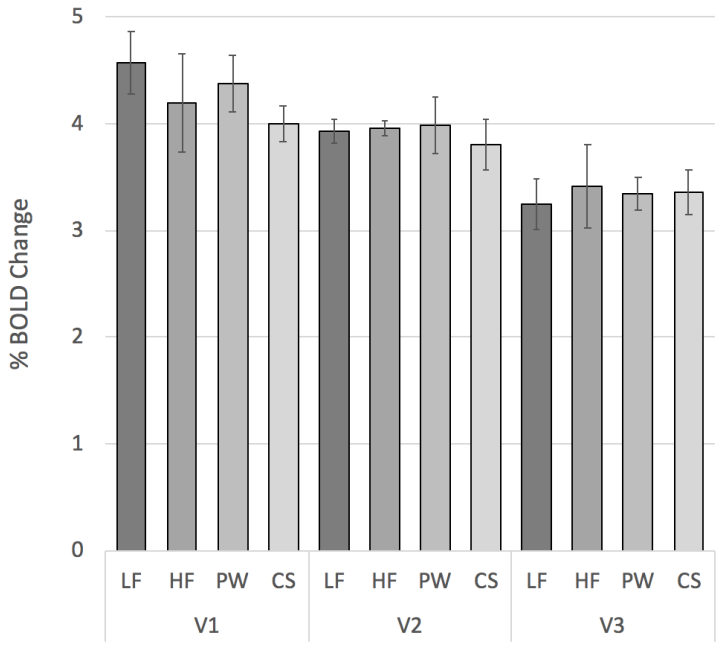



*Figure 36. Area effect size in the central ROI for each of the four conditions.*

Finally, a comparable analysis looked at task effects specifically in the central regions of the early visual areas and found a trend towards a main effect of Task [F(3,9)=3.455, p=0.065] but it was not significant and there were no significant interactions [all p>0.256].

## 3.7. Discussion

In this experiment, neural activity in V1-V3 was measured and compared with activity in vOT as participants performed a set of four different reading tasks, each designed to emphasize different aspects of reading. To see if linguistic factors influence processing in these early visual areas, the low-level visual properties of the stimuli were controlled while the higher-

level phonological, semantic, and lexical properties of the tasks and stimuli were manipulated.

The reading tasks all strongly engaged V1-V3 bilaterally. Of all the areas, V1 responded most strongly. From V1, activation decreased with each subsequent stage up the putative visual hierarchy until vOT where in the left hemisphere, but not the right, this trend reversed and activation was greater than in the preceding stage (i.e. V3). This was the only hemispheric asymmetry observed. This general pattern of decreasing activation (BOLD response) from V1-V3 is not out of line with expectations. Of the early visual areas, V1 has the highest vascular density (Zheng, LaMantia, & Purves, 1991) is the most neuron-dense (Collins, Airey, Young, Leitch, & Kaas, 2010).

Activation was strongly bilateral throughout not only the early visual areas but also vOT. However, in this region there was a significantly stronger response in the left relative to the right hemisphere. Greater activation in left vOT is consistent with neurological accounts that describe a preferential role for left vOT during reading (Cohen & Dehaene, 2004; Cohen et al., 2000; Dehaene et al., 2005; Vinckier et al., 2007). It is important to note, though, that this was a relative increase in BOLD signal – both left a*nd* right vOT showed significant activation for centrally presented words.

Within vOT (bilaterally), neural responses were not the same across the different tasks. Despite using the same stimuli, lexical decisions elicited stronger activation than the phonological decisions task, raising the possibility that higher-order properties relating to the linguistic actions being performed may be factor into the processing within the region.

There are, however, some differences between the two tasks that are worth considering. First, the phonological task did not include consonant strings so the stimuli were not exactly the same and, second, responses were far less frequent during the phonological task as participants only responded when target stimuli appeared rather than to every trial like they did in the lexical decisions task. Consonant strings, of all the conditions, evoked the strongest response in the vOT so could very well be a factor in this observed effect. However, it is unlikely to fully account for the difference as consonant strings were also included in the covert reading (and semantic decisions) task, and this task had comparable activation to that of the lexical decisions task. Covert reading also provided a control for the second point as the task did not require any overt responses. Considered together, this indicates that there is more to the task effects than differences in response frequency or the inclusion of the consonant strings.

Task effects have been previously reported in left vOT (Hellyer et al., 2011; Mano et al., 2013; Yang & Zevin, 2014). Mano and colleagues (2013) found that words and pseudowords elicited significantly stronger activation than consonant strings when the task required orthographic-phonological mapping (overt naming) but not when the task involved a non-linguistic visual decision (brightness judgment). Further, pseudowords elicited a stronger vOT response than words in the same region but only in the overt naming task. When Yang and Zevin (2014) investigated whether different task demands modify vOT sensitivity to words and other stimuli they found that the lexical decisions task elicited a stronger effect in the region than did the symbol detection task (press button if see '%'). Together these findings, along with the current results, suggest that different task demands on semantic, phonological, and orthographic processing (or simply just task difficulty and attentional

demands) can change how words are processed in vOT during reading. There was no evidence, however, of task effects influencing processing in the early visual areas (V1-V3).

The vOT response also varied by condition (see Figure 34). Low frequency words elicited a significantly stronger response than high frequency words, replicating the frequency effect found in previous fMRI studies (Chee, Westphal, et al., 2003; Kronbichler et al., 2004). Participants also responded significantly slower to low frequency than high frequency words, another widely reported frequency effect, although differences in response latency are unlikely to account for these differences in neural response as both pseudowords and consonant strings had even greater activation despite having slower and faster response times respectively.

In terms of V1-V3, the task or stimuli manipulations did not significantly modulate activity suggesting that these areas might be too early for such linguistic effects. Alternatively, the methods applied here may still lack the sensitivity to spot them. In that regard, a few limitations should be acknowledged. First, although not quantified, there was high inter-participant variability in task activation. Second, and relatedly, the sample size was small and even though power was increased by including a high number of trials along with analysis based in participant space, four participants may not be adequate to spot what could be small and subtle effects. Those limitations aside, these early areas may simply be too early for linguistic task and stimuli manipulations to be a factor. This question is explored in the next chapter when the neural responses in other ventral and dorsal area are investigated.

A conspicuous finding in V1-V3 was that reading elicited a strong response not only in the central foveal and parafoveal regions, encompassing to the expected location of the stimuli, but also in peripheral regions far beyond the retinal extent of the stimuli. Because literate adults have extensive training with sentential reading, it is possible that this peripheral activity could be driven bottom-up via learned associations between foveally and para-foveally presented words. When we read sentences, information from the fixated word arrives in foveal visual cortex but reading is facilitated by information in the parafovea (Rayner, 1998), presumably accounting for the well-known right visual field advantage, at least in languages that read left-to-right (Mishkin & Gorgays, 1952). An alternate hypothesis is that peripheral visual areas receive top-down modulation that is distinct from the bottom-up retinal stimulation (but is not modulated by these linguistic task or stimuli manipulations). One approach for testing this hypothesis is to have the same participants perform the same reading tasks again but this time with a set of non-word stimuli that have similar low-level spatial properties as the original stimuli but, crucially, lack any linguistic associations. Using a Japanese alphabet (Katakana), I created such a non-word stimulus set and had the same participants, all Japanese illiterates, perform the covert reading tasks again. Due to technical issues and time/costs constraints, I was unable to test all four participants. Preliminary results are described in

Appendix A. Other theories for the strong peripheral activation are explored in greater detail in Chapter 5.

The results of this investigation suggest that reading preferentially engages left vOT and that within this region, linguistic task and condition manipulations are a factor in processing even when low-level differences in visual form are tightly controlled. In contrast, areas V1-V3 do not appear to be influenced as a whole by these manipulations and top-down activation may not be a significant factor in areal processing until further along the ventral visual pathway.

# *4. Ventral and Dorsal Stream Contributions to Reading*

## 4.1. Introduction

As described in the previous chapter, reading strongly engaged the early visual cortices bilaterally however task and stimuli effects, evident in the left vOT, were not detected in these areas (V1-V3). This chapter investigates how the anatomically, and perhaps hierarchically, intermediate occipital areas between V1-V3 and vOT respond to the same stimuli and task manipulations. This intermediate region, situated posterior to the most posterior 'language areas', has received relatively little attention in terms of reading research and studies measuring how specific areas within this region respond to reading manipulations are rare. The prevailing assumption, roughly following the dual streams hypothesis (Goodale & Milner, 1992), is that during reading the ventral occipital areas are predominantly involved in recognising words (vision for perception) and dorsal areas are primarily involved in spatial processing including guiding eye-movements and allocating attention (vision for action). Neurological models of reading make little (Dehaene et al., 2005) or no mention (Price and Devlin, 2011) of the dorsal route at all, consistent with the implicit assumption that the ventral processing stream is *the* relevant stream for word recognition, at least under normal reading conditions. As will be discussed, however, there is accumulating evidence that both the dorsal and ventral aspects of this intermediate occipital region play a more complex role during reading than previously thought. The object of this chapter is to investigate how a set of retinotopically defined areas within this region respond to the reading tasks used the previous chapter so I can assess whether processing within these putative streams is modulated by higher-level factors and how dorsal and ventral activity compares more broadly.

### 4.1.1. Ventral regions of interest

Visually presented words elicit a strong response across the ventral occipital-temporal region not only in vOT, but also in the surrounding and more posterior cortex extending back to V3 (see Chapter 3; Yeatman et al., 2013). This intermediate region contains several distinct visual areas, although it should be noted that the criteria for defining these regions remains contentious (Brewer, Liu, Wade, & Wandell, 2005). Immediately posterior to vOT, three visual field maps, hV4 (hereafter V4), VO-1 and VO-2, can been identified (Brewer et al., 2005; Wandell et al., 2007; Wandell & Winawer, 2011). V4, according to the LCD model (Dehaene et al., 2005), is an intermediate stage along the ventral visual hierarchy that encodes case-specific letter patterns from the letter fragments (contours) that are extracted in V2. These case-specific letter representations then converge in VO/V8, forming abstract, case-invariant letter detectors. From there, the letter codes in left and right VO (covering the right and left hemifields respectively) converge on left vOT, forming abstract word form detectors (Dehaene et al., 2005). The VO circuits, however, have recently been shown to integrate the hemifield representations of foveal-split words (Strother, Coros, & Vilis, 2016), a union not thought to take place until vOT (Cohen et al., 2002) and furthermore, this VO/V4 region appears to be sensitive to the properties of letters *combinations* like bigram typicality (Woollams et al., 2011) suggesting that processing in this region extends beyond the encoding of individual letters. Previous investigations into the ventral contributions to reading have rarely mapped the areas posterior to the vOT (although see Yeatman et al., 2013) and systematic investigation into how these individual areas respond to different reading demands is lacking. In this chapter I analyse the activity in retinotopically defined

VO-1, VO-2, and V4 during reading to assess whether these areas, like the left vOT, are sensitive to higher-level task and stimuli manipulations.

### 4.1.2. Dorsal regions of interest

While research into the early neural stages of reading have mostly focused on ventral structures, visually presented words have been found to elicit a strong response in more dorsal occipital-parietal regions, especially under more demanding reading conditions. When Cohen et al. (2008) compared the neural response to normally and abnormally presented words in a semantic decisions task, they found that the abnormal words activated several occipito-parietal regions that were not active under the normal reading conditions. Specifically, a bilateral region in the intraparietal sulcus (IPS/V7) responded more strongly regardless of the which of three abnormality conditions (word rotation, letter spacing, and word position) were shown. Further, an earlier MEG study using a lexical decisions task (Pammer, Hansen, Holliday, & Cornelissen, 2006), found that the V7 region responded more vigorously to words degraded by shifting letters randomly above and below the midline.

Dorsal involvement also appears to extend to more typical presentations. For example, occipital-parietal activation is stronger for MiXeD-cAsE than normally written words (Mayall, Humphreys, Mechelli, Olson, & Price, 2001) and even for pseudohomophones relative to exception words (Borowsky et al., 2006), perhaps indicating that dorsal structures play a role in 'normal' reading conditions. Consistent with this view, when Richardson and colleagues (2011) used dynamic causal modelling to evaluate the flow of information from

visual cortex into the cortical language system during single word reading, their results demonstrated separable routes from V1, either ventrally through vOT or dorsally through the temporo-parietal junction. These and other findings suggest that the dorsal visual stream may play an important role in reading, perhaps involving the spatial and attentional processes needed for the serial scanning of letters. In this chapter I analyse how retinotopically defined V7, V3a, and V3b respond during reading in order to investigate how their activity compares to activity in the ventral areas and to also assess whether these dorsal areas are sensitive to higher-level task and stimuli manipulations.

Although no longer strictly considered a dorsal stream structure (Gilaie-Dotan, 2016), area MT (hereafter V5), a motion sensitive area in the middle temporal region (Tootell et al., 1995), also appears to play an important role in reading. For example, activity in MT correlates with reading performance both in adults (Demb, Boynton, & Heeger, 1998) and in children (Ben-Shachar, Dougherty, Deutsch, & Wandell, 2007). In children, the strength of V5 activation was strongly correlated with phonological awareness and to a lesser extent with two other reading proficiency measures (Ben-Shachar et al., 2007). Moreover, in children with reading-specific difficulties (i.e. developmental dyslexics), abnormal activation of V5 has been widely reported as a possible source of their reading difficulties (Eden et al., 1996; Stein & Walsh, 1997).

As with the investigations into the ventral contributions to reading, retinotopic mapping procedures are rarely used in reading research and this lack of accurately defined dorsal areas make the comparison and interpretation of results more difficult. The V5 region for example, is a cluster of small but distinct visual areas with different response profiles (Zeki,

2015) and its anatomy is highly variable across individuals (Dumoulin et al., 2000; Huk, Dougherty, & Heeger, 2002). Given its potentially important role in reading, this area was included as a region of interest.

### 4.1.3. Specific questions

My aim in this chapter is to determine the extent to which dorsal structures are engaged in reading, relative to ventral structures, and to investigate if visual word processing across these two streams is better characterised as feedforward-only or bi-directional. To do this I first examined the activation maps for reading across the dorsal and ventral areas. I then quantitatively compared BOLD response between the two streams to determine if reading primarily engages ventral structures, as assumed by contemporary neurological models of reading. Next, I looked for effects of the different reading tasks on activation within the dorsal and ventral visual areas to determine whether those manipulations significantly affected activity in those areas as they did in the vOT (see previous chapter). Finally, I analysed the data from the early visual, dorsal, and ventral areas using Dynamic Causal Modelling (DCM; Friston et al., 2003) in order to investigate how neuronal activity in these areas is interrelated and to assess whether processing across this network is better explained by a feedforward or interactive model.

## 4.2. Methods

The data in this chapter come from the four reading (i.e. covert reading, lexical decisions, phonological decisions, semantic decision) but not the one-back task, which is reported separately in Chapter 5. A full description of the data collection and image analyses used here can be found in the General Methods chapter. In brief, ROIs for V5 and ventral areas V4, VO-1, and VO-2 and dorsal areas V3a, V3b, and V7 were defined retinotopically in each hemisphere (see section 2.7 in General Methods for more information).

The first statistical analysis compared ventral (V4, VO-1, VO-2) and dorsal (V3a, V3b, V7) activity during reading using a 2 × 2 ANOVA with Hemisphere (left, right) and Stream (dorsal, ventral) as independent factors to determine whether there were any differences in activation between the two visual streams and whether this varied by hemisphere. The dependent measure was mean effect size calculated as the percent BOLD signal change from the voxels 'activated' by the contrast of the four stimuli categories relative to rest. Activation was determined using a voxel-wise threshold of $Z>2.3$ (or $p<0.01$ uncorrected for multiple comparisons).

The second analysis investigated whether stimulus condition influenced activity in the dorsal and ventral streams using a 2 × 2 × 4 ANOVA with Hemisphere (left, right) and Stream (dorsal, ventral) and Stimuli (low frequency, high frequency, pseudowords, consonant strings) as independent factors. Post-hoc, pairwise comparisons used a Bonferonni correction to adjust family-wise error for multiple comparisons.

A third analysis investigated how individual areas within the ventral stream responded to the different stimuli conditions using two 2 × 3 × 4 ANOVA with Hemisphere (left, right), Area (V4, VO-1, VO-2), and Stimuli (low frequency words, high frequency words, pseudowords, and consonant strings) as factors. The same analysis was also run for the dorsal stream.

Additionally, to investigate whether high-level task requirements influenced neural activity, the second and third analyses described above were also run using Task (lexical decisions, semantic decisions, phonological decisions, and covert reading) instead of Condition as a factor.

Finally, DCM was used to determine whether the BOLD signal evidence better supports a feedforward or an interactive model of the functional connections between the primary visual cortex and dorsal and ventral visual areas. In addition, the analysis evaluated the strength of evidence for each functional connection between the nodes of the models, including lateral links between the dorsal and ventral streams.

## 4.3. Results

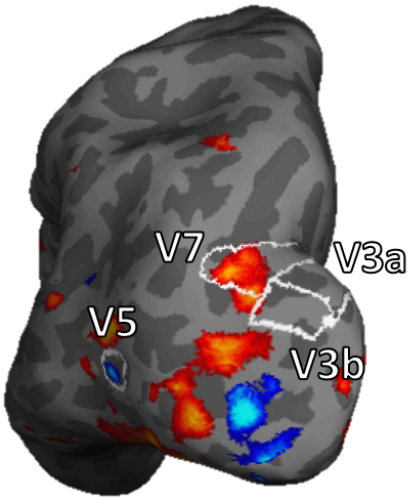
### 4.3.1. Bold response

Figure 37 shows how the different visual areas responded to words during the covert reading task. In all participants, words strongly engaged the ventral areas bilaterally, with clusters of significant activation typically found throughout the ventral surface between the

ventrolateral aspect of V3 and vOT where the peak response was often found. Dorsally, there was strong bilateral activation in the dorsomedial region extending from V3a/V3b to V7 and into the dorsal parietal lobe, just medial to the intraparietal sulcus. In addition, there was also a strong response in a more inferolateral region, situated between the posterior aspect of V5 and the anterolateral aspect of V3, likely overlapping the lateral occipital complex (Brewer et al., 2005). In V5, the response to words was relatively weak and was not consistently active during the reading task (relative to fixation).

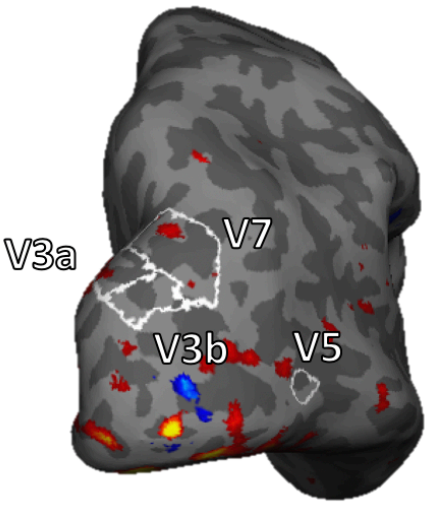
*Participant 1*

*A*

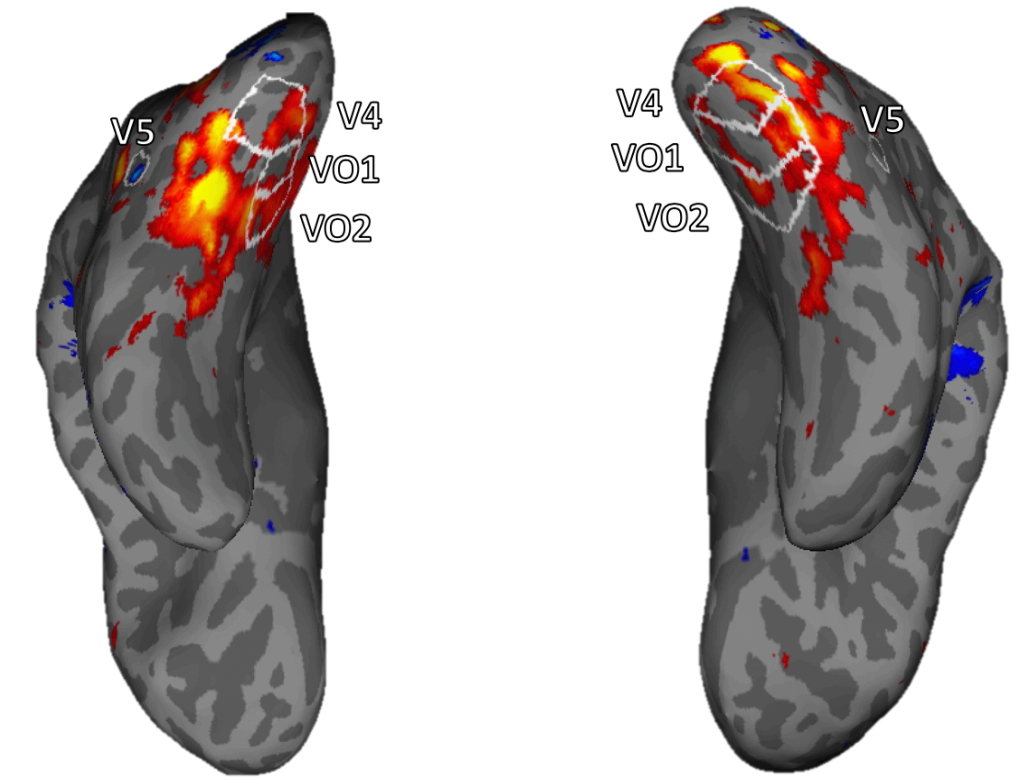



*B*

*C*

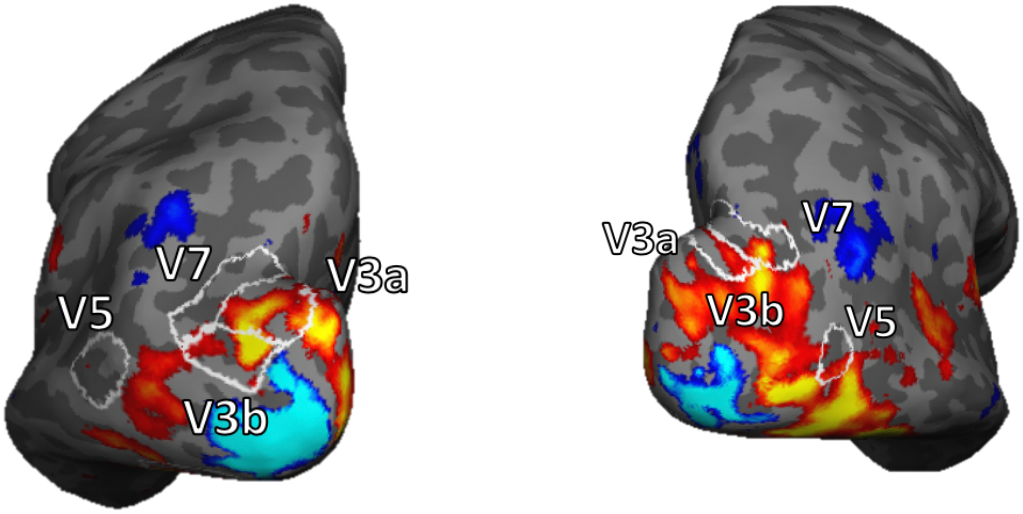



*D*

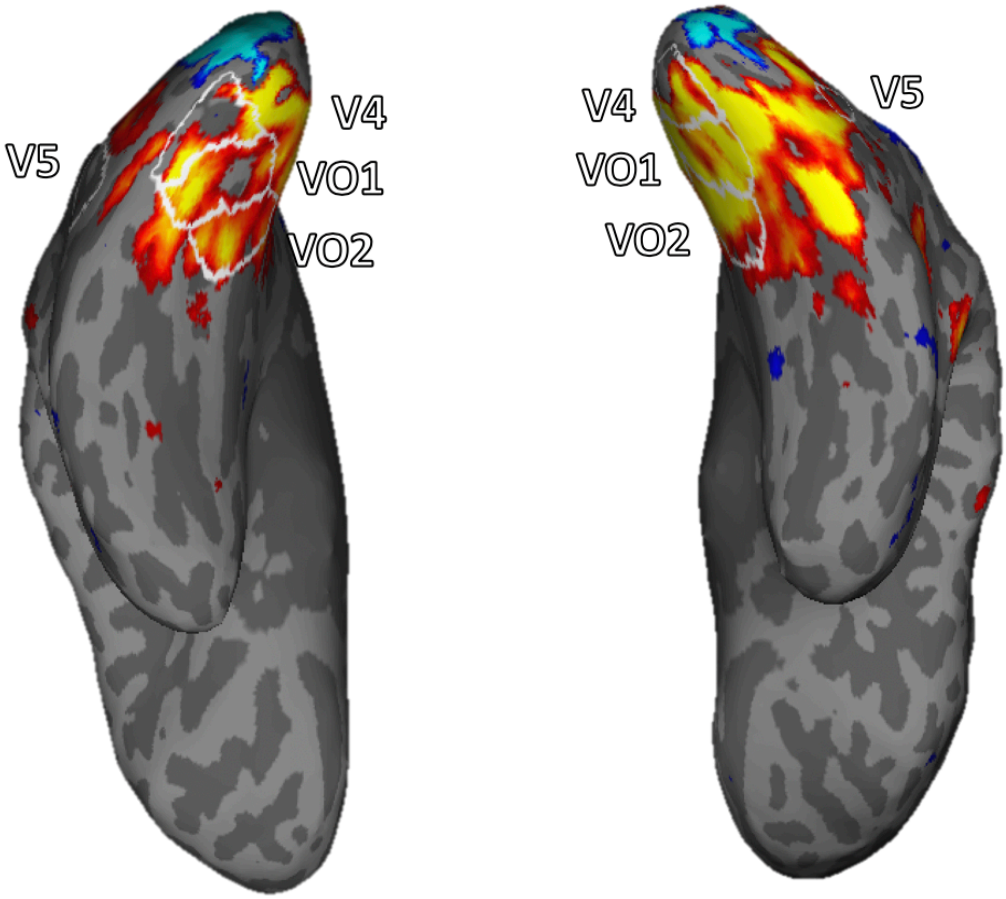



*Participant 2*

*A* *C*

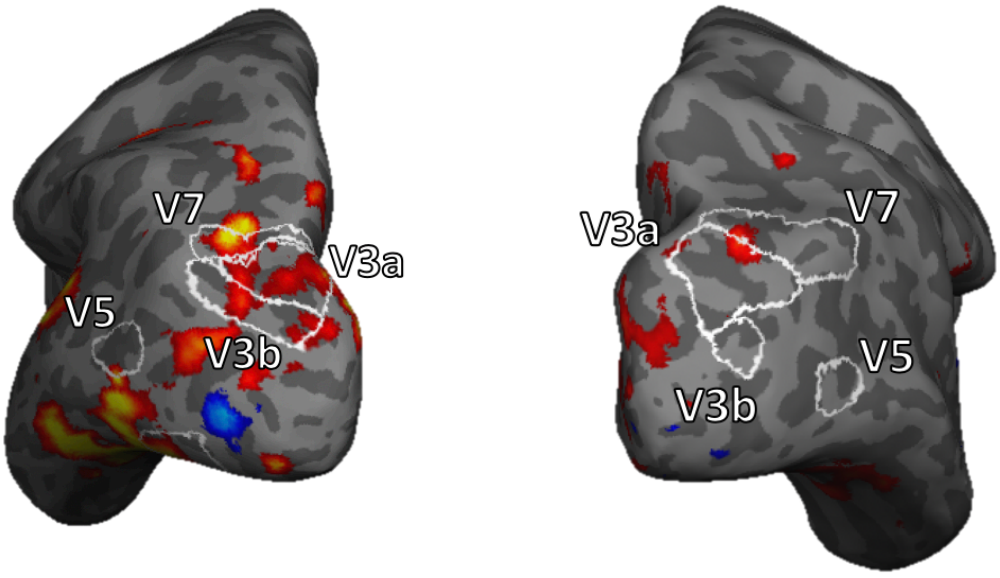



*B* *D*

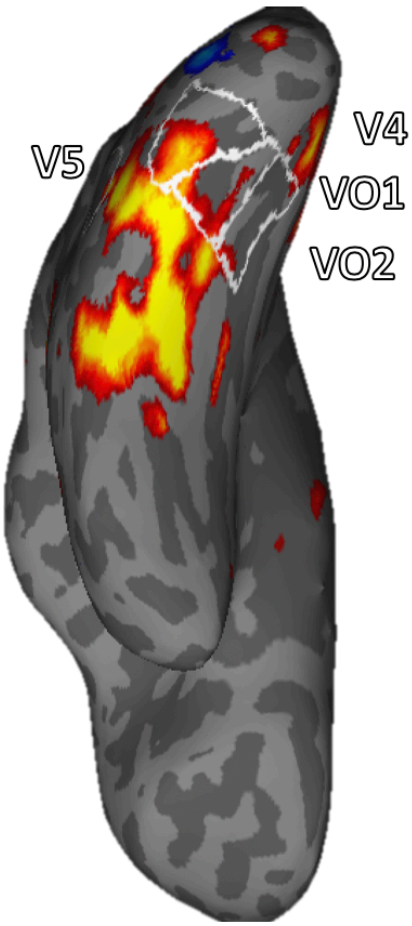


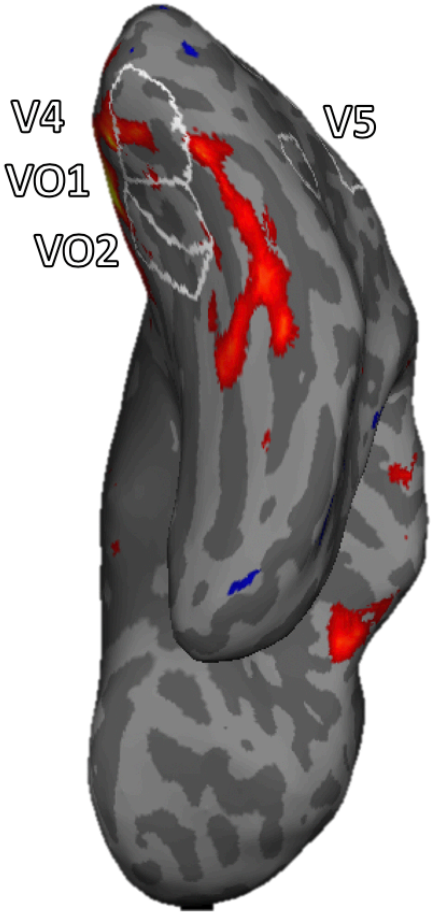

*Participant 3*

*A* *C*



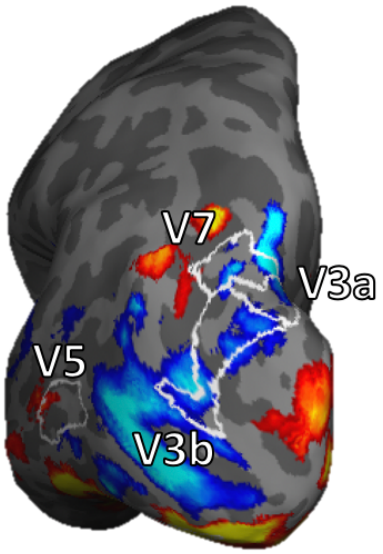

*B* *D*

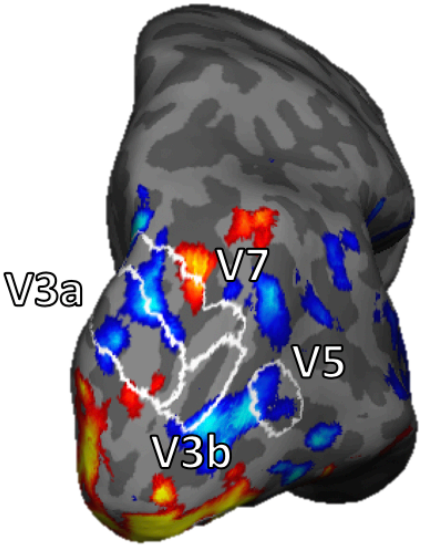



*Participant 4*

*A* *C*




*B* *D*

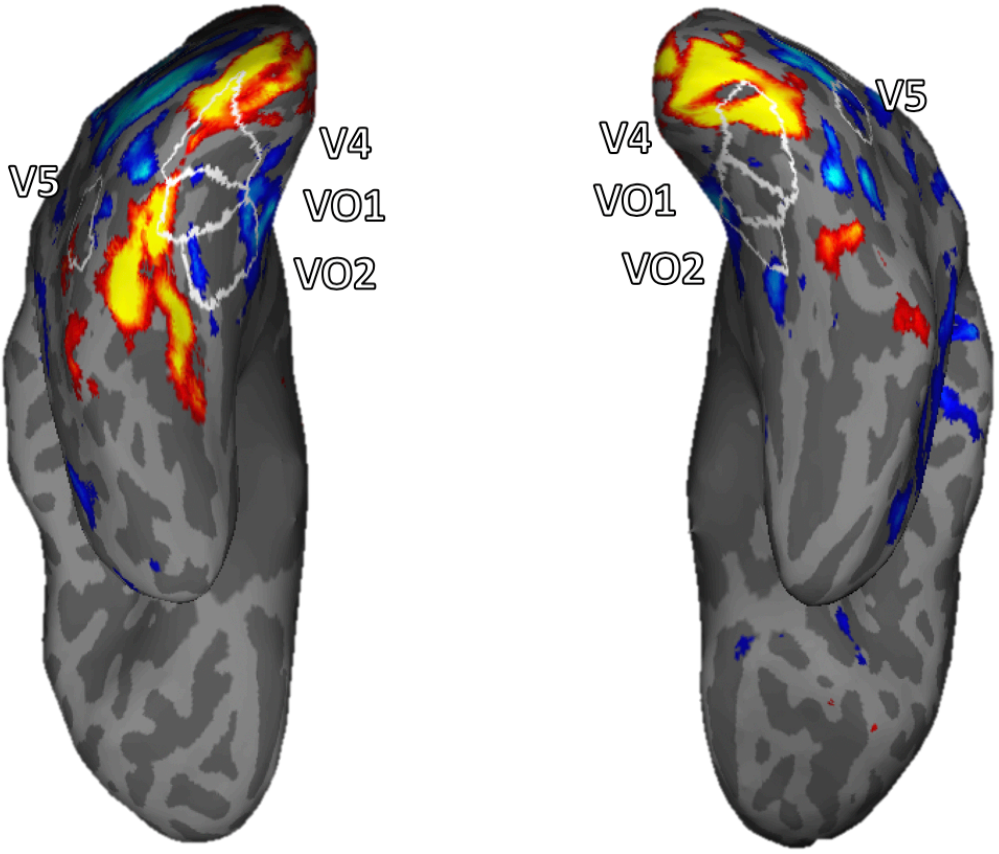



*Figure 37. Activation (words > rest) during the covert reading task overlaid on each participant's inflated left and right hemisphere. (A,C) Dorsal view of left and right hemispheres, respectively, with the borders of V3a, V3b, V7, V5 shown in white. (B, D) Ventral view of left and right hemispheres, respectively, with the borders of area V4, VO-1, VO-2, VOT shown in white. Activations are thresholded at Z>2.3*

Before investigating if the different task and stimuli manipulations influenced neural activity, each area was checked to see how many of its voxels were active during reading. In chapter three, effect size was calculated as the mean signal across all active voxels (Z>2.3) and before the same approach was applied here, the size of the masks (i.e. the number of active voxels) were compared to the overall size of the areas to make sure that analysis was not based on a trivial number of voxels. For each area, an average mask size was calculated (across stimuli conditions and tasks) and compared to the total number of voxels. As can be seen in Figure 38, ventral areas and the vOT had a high percentage of active (masked) voxels, often as high or higher than in areas V1-V3. The percentages were lower in the dorsal areas but the masks still, at a minimum, included more than 10% of all voxels. In area

V5, the percentage of active voxels was considerably lower. On closer inspection, V5 was not consistently active during reading and participants often did not have any active voxels for one or more reading tasks. As a result of this inconsistent engagement, V5 was not included in further analysis.

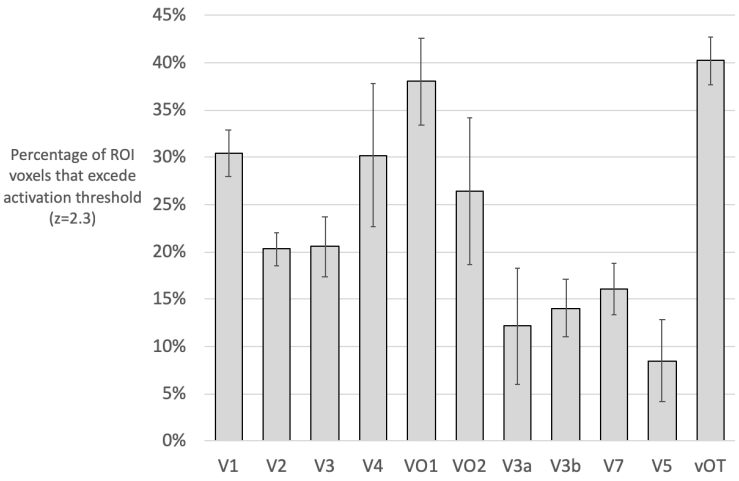



*Figure 38. Average percentage of voxels within each ROI that exceeded the activation threshold (z=2.3). For each ROI (per participant), the proportion of supra-threshold voxels was calculated for each task/condition and then averaged together across hemispheres and then participants. As only the supra-threshold voxels within an ROI were included in the subsequent reading analysis (see below), it was important confirm that that analysis was not based on a trivial proportion of voxels (note: V5 was excluded from the reading analysis for reasons described below). As can be seen, the remaining ROIs had, on average, more than 10% of their voxels included the analysis. Error bars represent the standard deviation.*

To investigate how the different visual areas responded during reading, mean effect size was calculated across all tasks and stimuli conditions (Figure 39A). In both hemispheres, the three ventral areas (V4, VO-1, VO-2) showed a similar pattern. Effect size was largest in V4 and decreased from VO-1 to VO-2 where the effect size was smallest (Figure 39A). There were comparable sized effects in the dorsal areas. Across hemispheres (Figure 39B), effect size increased from V3a, to V3b and to V7 where effect size was largest.

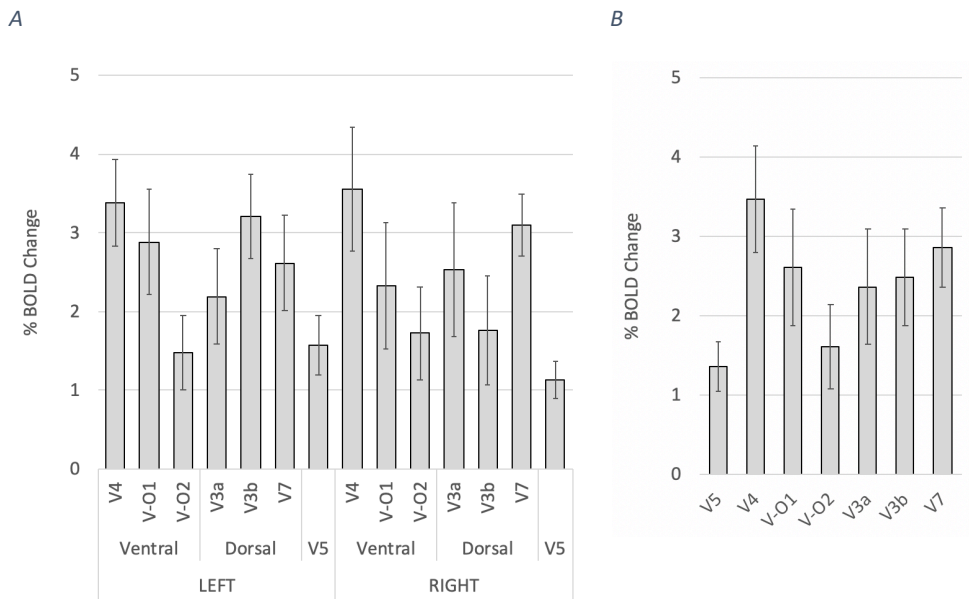



*Figure 39. Area effect size collapsed over the all tasks and conditions. (A) Area effect size by hemisphere. (B) Area effect size across hemisphere.*

To compare ventral (V4/VO-1/VO-2) and dorsal (V3a/V3b/V7) stream activity, the mean effect sizes were entered into a 2 × 2 ANOVA with Hemisphere (left, right) and Stream (ventral, dorsal) as independent factors. The analysis showed that there were no main effects of Hemisphere [$F(1,3)=0.400$, $p=0.572$] or Stream [$F(1,3)=0.003$, $p=0.959$] and no significant interactions ($p>0.176$) indicating that both the ventral and dorsal streams were engaged by the reading tasks and there was no evidence of difference between the left and right hemispheres.

To investigate if ventral (V4/VO-1/VO-2) and dorsal (V3a/V3b/V7) stream activity was influenced by the different stimuli conditions, mean effect sizes were entered into a 2 × 2 × 4 ANOVA with Hemisphere (left, right), Stream (dorsal, ventral), and Stimuli (low frequency, high frequency, pseudowords, consonant string) as independent factors. The analysis revealed a main effect of Stimuli [$F(3,9)=7.803$, $p=0.007$]. Numerically, high frequency words showed the least activation followed by low frequency words, pseudowords and then

consonant letter strings. Post-hoc comparisons between the four conditions, however, revealed no significant differences after Bonferonni correction (all p>0.12). There were no main effects of Hemisphere [F(1,3)=0.464, p=0.545] or Stream [F(1,3)=0.089, p=0.785] and no significant interactions (p>0.214) indicating that the condition influenced activity in both streams and in both hemispheres.

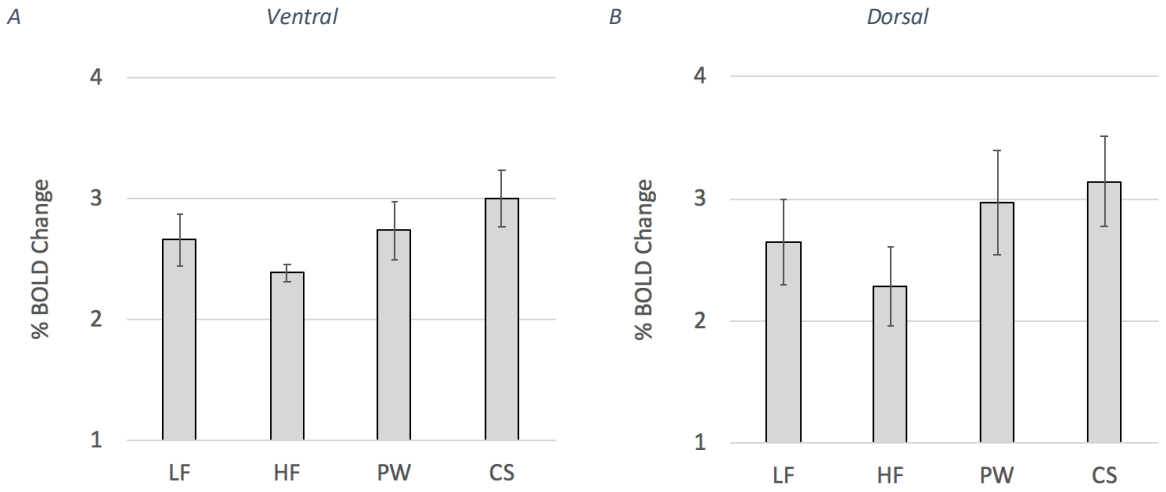



*Figure 40. Dorsal and ventral area effect sizes for each stimuli condition (across task and hemisphere). (A) Effect size across ventral areas (V4, VO-1, VO-2). (B) Effect size across dorsal areas (V3a, V3b, V7).*

To investigate whether the individual areas within each stream responded to the different stimuli conditions, two ANOVAs were calculated, one for each stream. The first investigated the ventral visual stream with a 2 × 3 × 4 ANOVA with Hemisphere (left, right), Area (V4, VO-1, VO-2), and Stimuli (low frequency words, high frequency words, pseudowords, and consonant strings) as factors. This analysis revealed a main effect of Stimuli [F(3,9)=3.864, p=0.050] but no main effects of Hemisphere [F(1,3)=0.005, p=0.950] or Area [F(1,3)=2.185, p=0.194] and no significant interactions (p>0.520 uncorrected). The second investigated the dorsal visual stream with a 2 × 3 × 4 ANOVA with Hemisphere (left, right), Area (V3a, V3b, V7), and Stimuli (low frequency words, high frequency words, pseudowords, and consonant strings) as factors. This analysis also revealed a main effect of Stimuli [F(3,9)=9.755,

p=0.003] with no significant main effects of Hemisphere [F(1,3)=0.289, p=0.628] or Area [F(1,3)=0.218, p=0.810] and no significant interactions (p>0.225 uncorrected). In both cases, the pattern of activation was consistent with the overall pattern reported above (see Figure 40). In other words, there was a significant effect of Stimuli that was consistent across streams and across regions within each stream.

The final analysis investigated whether there were any significant Task (lexical decisions, semantic decisions, phonological decisions, and covert reading) effects in these higher order visual areas and whether they were influenced by Hemisphere (left, right) or by Stream (ventral, dorsal). The ANOVA revealed no significant main effects or interactions involving Task, indicating that the high-level task differences did not influence neural activity across the dorsal and ventral streams.

### 4.3.2. DCM

All of the DCM analyses described below used four regions-of-interest: the central foveal/parafoveal part of V1 (V1c), the peripheral part of V1 (V1p), a dorsal region comprised of V3a, V3b, and V7, and a ventral region comprised of V4, VO1, and VO2. In theory, it is possible to model each of the visual areas as separate ROIs but in practice this would involve a total of 16 nodes (the two V1 areas, three dorsal regions, and three ventral regions in each hemisphere) which becomes computationally intractable (Stephan et al., 2010). Because the questions investigated here focused on differences between the dorsal and ventral streams, it was possible to simplify the model by combining the individual areas into a dorsal and ventral ROI. This also avoided the issue of a given dorsal or ventral region

not having any 'active' voxels (i.e. Z>2.3) within an individual participant, which would preclude using that region in the model. In contrast, I chose to separate V1 into central and peripheral ROIs in order to help distinguish the sources of the unexpected peripheral activation found during reading (see Chapter 3). Given the hypothesis that V1p may be receiving top-down feedback from non-visual areas, separating V1 into central (stimulated) and peripheral nodes provided an opportunity to explicitly test whether the peripheral activation was solely driven by bottom-up input from V1c or whether there was significant top-down modulation as well. Finally, it is important to note that the data from the left and right hemispheres were modelled together. That is, each ROI included both the left and right hemisphere areas. This bilateral model approach was motivated by the lack of hemisphere effects found in any of the above analyses (see section 4.3.1).

Three different models were built from these four ROIs. In each case, the central (foveal and parafoveal) coding region of V1, where the word stimuli would have appeared, received the experimental input. The Forward Model included a full set of feed-forward connections linking V1c $\rightarrow$ V1p, V1c $\rightarrow$ Dorsal, V1c $\rightarrow$ Ventral, V1p $\rightarrow$ Dorsal, and V1p $\rightarrow$ Ventral) while the Interactive Model also included top-down connections (Dorsal $\rightarrow$ V1c, Dorsal $\rightarrow$ V1p, Ventral $\rightarrow$ V1c, Ventral $\rightarrow$ V1p, and V1p $\rightarrow$ V1c) as well as lateral connections (Dorsal $\rightarrow$ Ventral and Ventral $\rightarrow$ Dorsal)(Figure 41). A third model implemented a null hypothesis that the regions do not interact at all. As a result, it did not include any connections between nodes, neither forward, backward, nor lateral. This was used as a control to determine whether there was sufficient evidence to reject the null hypothesis.

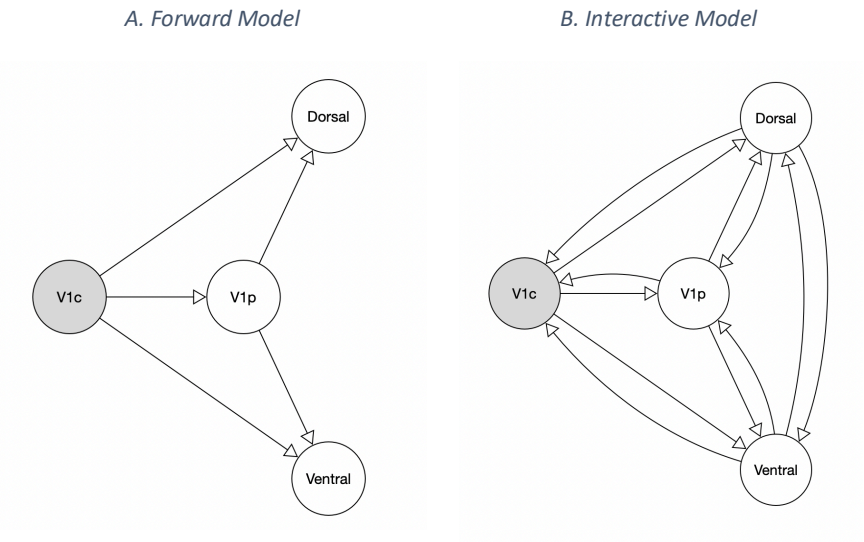



*Figure 41. Model space for Bayesian model comparison. (A) the forward model included fixed, unidirectional connections (represented by the arrows) between the foveal/parafoveal region of V1 (V1c) and the peripheral region of V1 (V1p), the dorsal area, and the ventral area. There were also unidirectional forward connections linking V1p and dorsal and ventral areas. (B) the interactive model included reciprocal connections between all areas. A null model (not shown) was also computed. In this model, areas were only connected with themselves.*

To begin, the fMRI covert reading data for the four participants were re-analysed in SPM (as opposed to FSL) so that the DCM analyses could be conducted using the SPM12 software package. Recall that the covert reading data included 5 separate sessions of data per participant. These were combined in a first level fixed-effects analysis by concatenating the volumes into a single 1825 volume time-series. The analysis consisted of a single condition contrasting written stimuli (i.e. LF, HF, PW, CS trials) with rest. These were modelled as delta functions convolved with a standard double-gamma HRF (Glover, 1999) in an event-related analysis. The estimated motion parameters were included as covariates-of-no-interest. A special SPM function (*spm_fmri_concatenate*) was run to adjust the high-pass filter and temporal auto-correlation estimates to correctly account for temporal discontinuities between sessions. In addition, it added session-specific regressors to compensate for changes in mean signal intensity across runs. The model was then estimated and the contrast Stimuli > Rest was calculated. Principle eigenvariates were extracted for

the V1c, V1p, dorsal, and ventral ROIs using the retinotopically defined masks for each individual.

Connections within the models were defined as bilinear and each node was modelled as a single state. In other words, there were not separate states for excitatory and inhibitory neuronal populations as is common when analysing MEG data with DCM (David & Friston, 2003). Stochastic effects were not included in the models (Daunizeau, Stephan, & Friston, 2012).

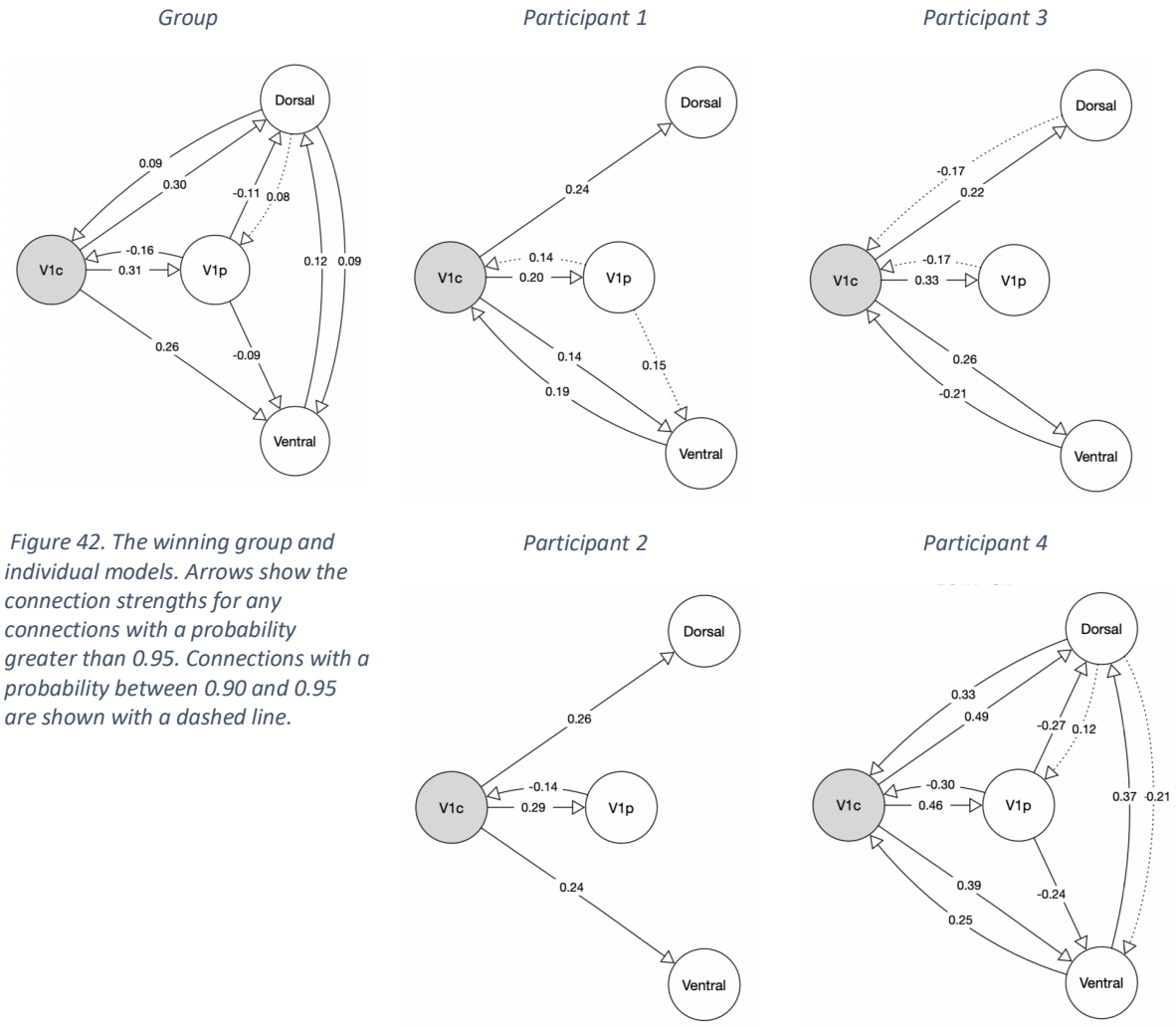
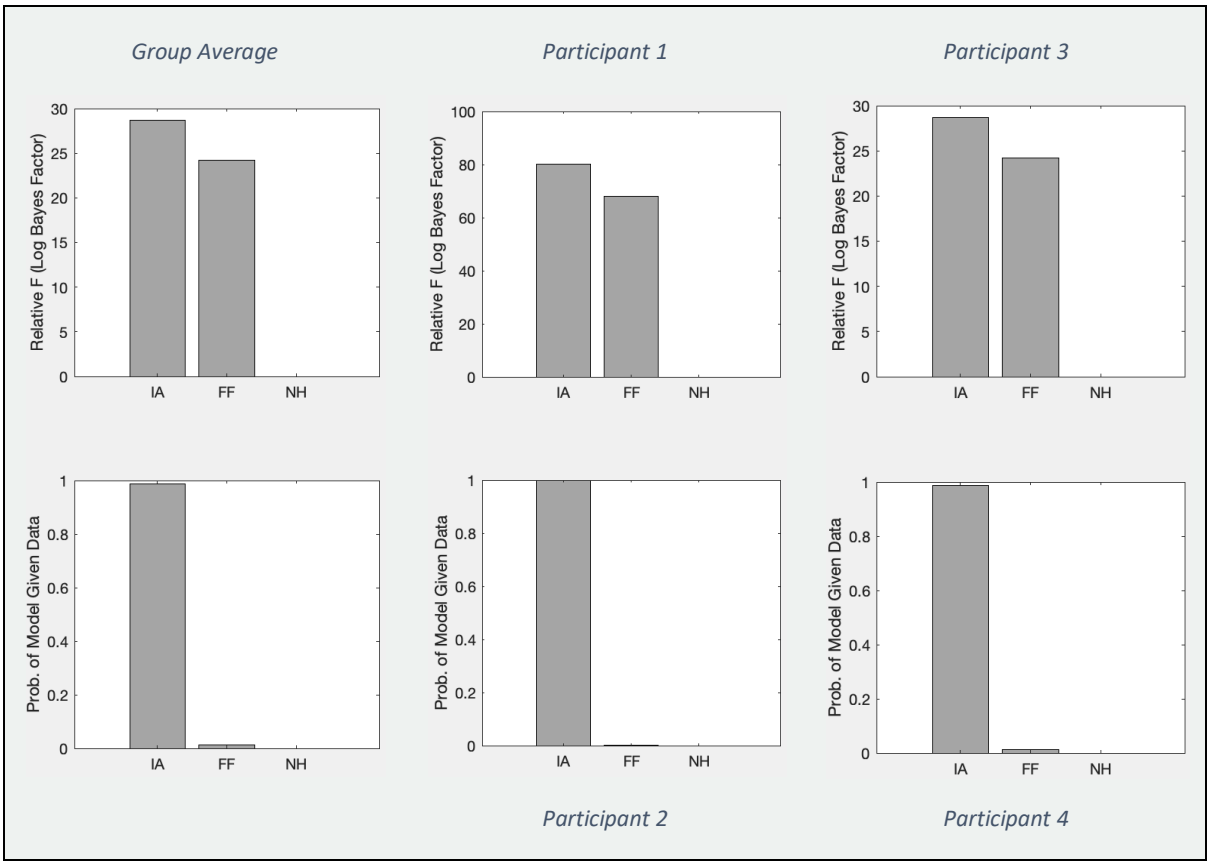



*Figure 42. The winning group and individual models. Arrows show the connection strengths for any connections with a probability greater than 0.95. Connections with a probability between 0.90 and 0.95 are shown with a dashed line.*

For each participant, the three models were estimated against the time series data. Bayesian model selection was used to compute the posterior probabilities over the models and then compare their performance using the relative log Bayes factor and the overall probability of model given the data. To compare how the models performed at a group level, the above parameters were averaged across the four fitted DCMs in a Bayesian Fixed Effects analysis. For each winning model, the connection strengths for any connections with a probability greater than 0.95 were reported (Figure 42).



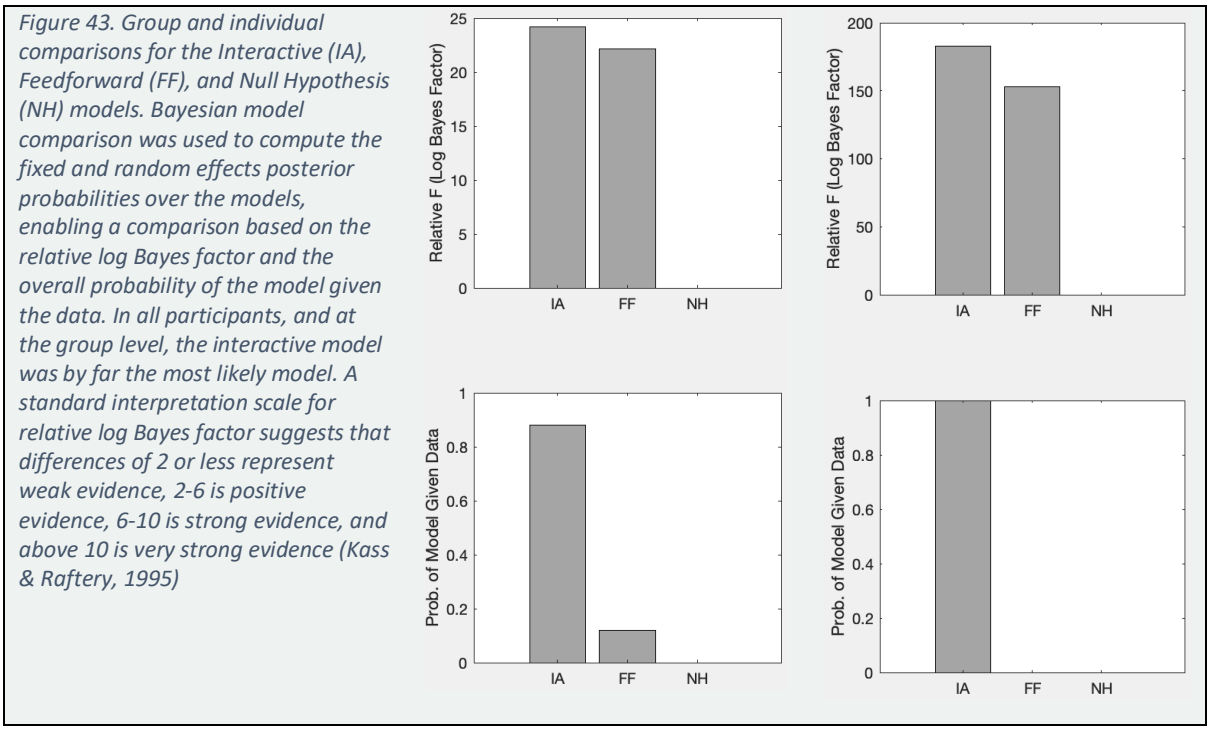



*Figure 43. Group and individual comparisons for the Interactive (IA), Feedforward (FF), and Null Hypothesis (NH) models. Bayesian model comparison was used to compute the fixed and random effects posterior probabilities over the models, enabling a comparison based on the relative log Bayes factor and the overall probability of the model given the data. In all participants, and at the group level, the interactive model was by far the most likely model. A standard interpretation scale for relative log Bayes factor suggests that differences of 2 or less represent weak evidence, 2-6 is positive evidence, 6-10 is strong evidence, and above 10 is very strong evidence (Kass & Raftery, 1995)*

At the group level, there was strong evidence for each of the feed-forward connections and nearly all of the feedback connections (see Figure 43). Connections with a 95% or greater probability of being present are shown as solid arrows whereas those with only a 90-95% probability are shown as dotted arrows. The only connections not to reach this threshold were the feedback connections from the ventral region to V1c and V1p. In other words, the model explained the functional imaging data best by including a combination of feed-forward and feed-back connections, as well as lateral connections linking the dorsal and ventral regions.

At the level of individual participants, most of the feed-forward connections were present in all four participants. That is, the connections from V1c to the three other regions (V1p, dorsal, and ventral) were present with 95% confidence. The feed-forward links from V1p to the dorsal and ventral regions were less consistent. Every participant also showed evidence of feed-back connectivity, although the connections reaching the 95% confidence level

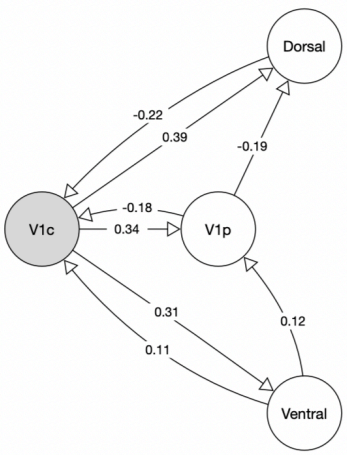
varied across individuals. Participant 2, for instance, only showed a reliable feed-back connection from V1p $\rightarrow$ V1c whereas Participant 4 showed reliable feedback from all three regions into V1c.

To formally evaluate the models, Bayesian model comparison was used to compute the fixed and random effects posterior probabilities over the models. Three models were compared: the Interactive model (IA) that included the full set of connections (feed-forward, feed-back, and lateral), the Feed-Forward model that only included the forward connections, and a Null Hypothesis (NH) model that did not include any links between regions. This latter model assumes that the regions are not interacting at all and the best explanation for the imaging data is that the regions are functionally independent. It is used to assess the strength of evidence in support of the two more realistic models. After estimating each model, the relative log Bayes factor ($\log_2[F]$) and the overall probability of the model given the data are computed (Stephan et al., 2007). As can be seen in Figure 43, the group evidence for the IA model was 28.7 whereas it was 24.2 for the FF model, a difference of 4.5. A standard interpretation scale for relative log Bayes factor suggests that a difference of 2 or less represent weak evidence, 2-6 is positive evidence, 6-10 is strong evidence, and above 10 is very strong evidence (Kass & Raftery, 1995). In the current case, there is positive evidence that the 'winning model,' that is the model that best explains the fMRI data, is the interactive model that includes feed-forward, feed-back and lateral connections. This is also reflected in the probabilities of each model. The IA model has a probability of 99% compared to the FF model (1%) and the null hypothesis (0%). In other words, the evidence from these DCM analyses strongly supports the presence of feed-back and lateral connections in addition to the uncontroversial feed-forward connections.

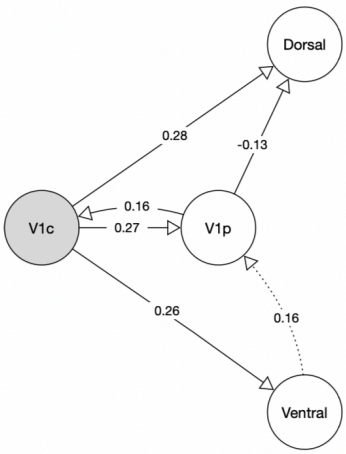
A strong assumption in these analyses, however, is that there are no differences between the left and right hemispheres, at least insofar as applies to these early visual cortices when processing written stimuli. This assumption is based on the lack of significant hemisphere effects in the previous analyses. That is, there was no evidence for a difference in the magnitude of activation between the left and right early visual cortices. As a result, the above DCM analyses combined left and right regions into a single ROI (e.g. V1c was composed of V1c-LH and V1c-RH). DCM analyses, however, do not measure activation magnitude but rather the interactions between regions represented by fluctuations in these magnitudes. As a result, it seemed prudent to conduct separate DCMs for the left and right hemispheres to investigate whether the combined results are representative or whether they hide important laterality effects. Shown below are the unilateral results for the left hemisphere (see Figure 44 and Figure 45) and right hemisphere (see Figure 46 and Figure 47).

*Left Hemisphere*

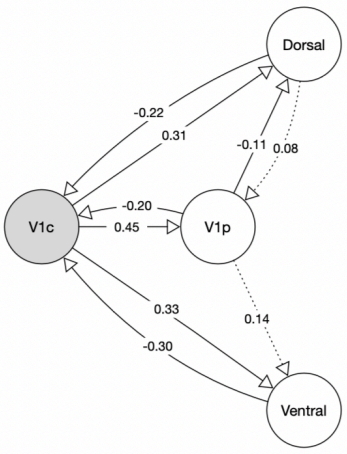
*Group Average*




*Participant 1*



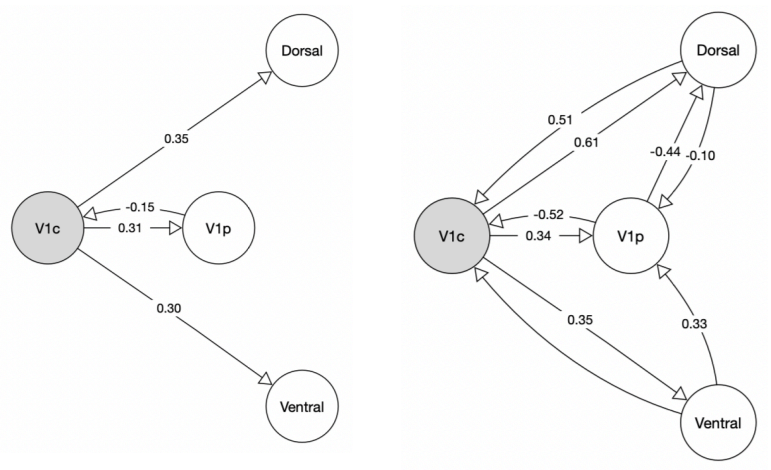

*Participant 3*




*Participant 2*

*Participant 4*

*Figure 44. The winning left-hemisphere group and individual models. Arrows show the connection strengths for any connections with a probability greater than 0.95. Connections with a probability between 0.90 and 0.95 are shown with a dashed line.*



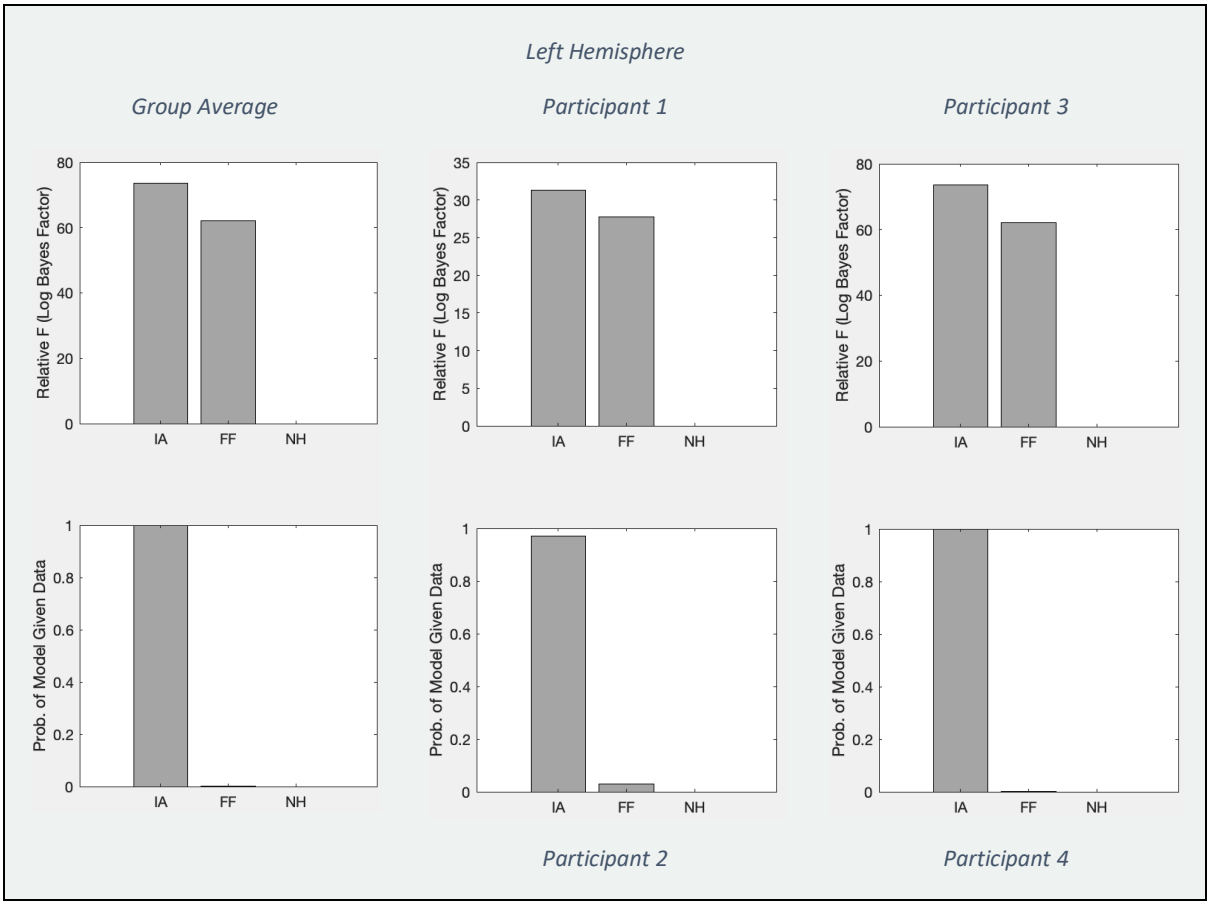
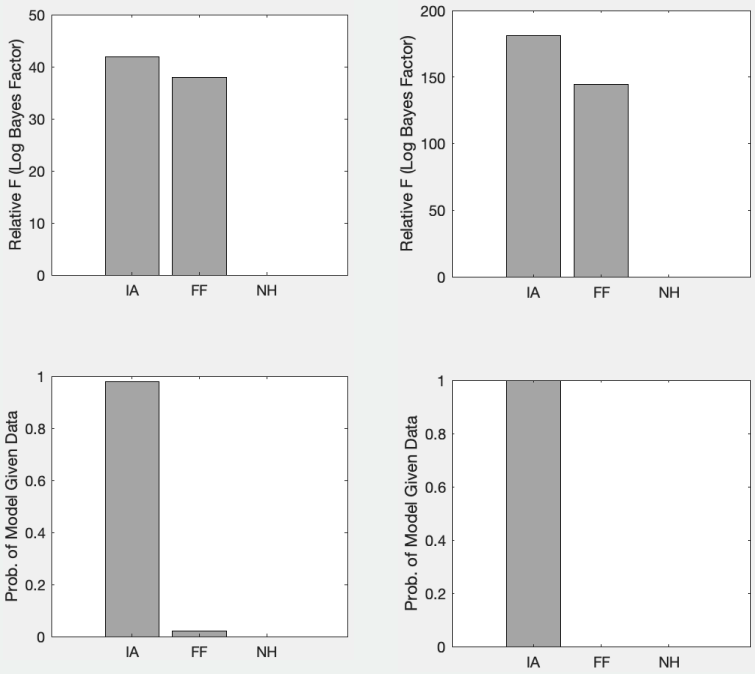
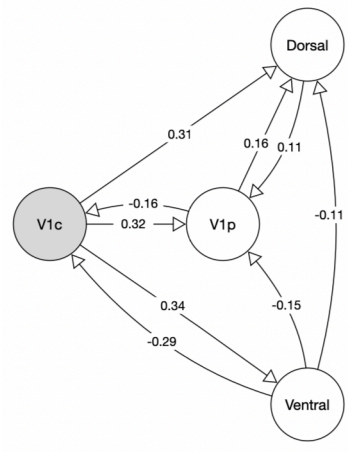



*Figure 45. Group and individual comparisons for left-hemisphere Interactive (IA), Feedforward (FF), and Null Hypothesis (NH) models.*

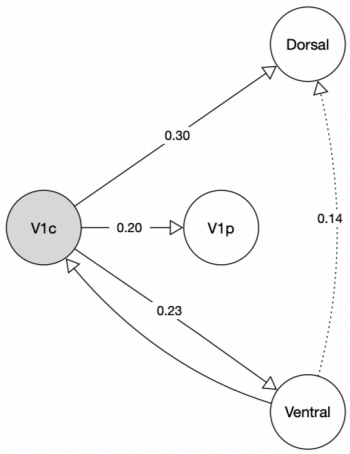



*Right Hemisphere*

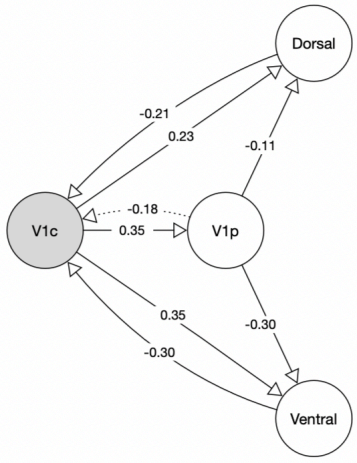
*Group Average*




*Participant 1*



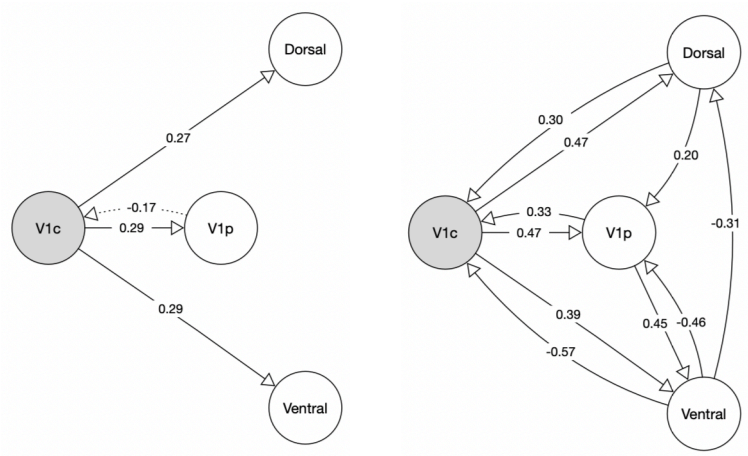

*Participant 3*




*Participant 2*

*Participant 4*

*Figure 46. The winning right-hemisphere group and individual models. Arrows show the connection strengths for any connections with a probability greater than 0.95. Connections with a probability between 0.90 and 0.95 are shown with a dashed line.*



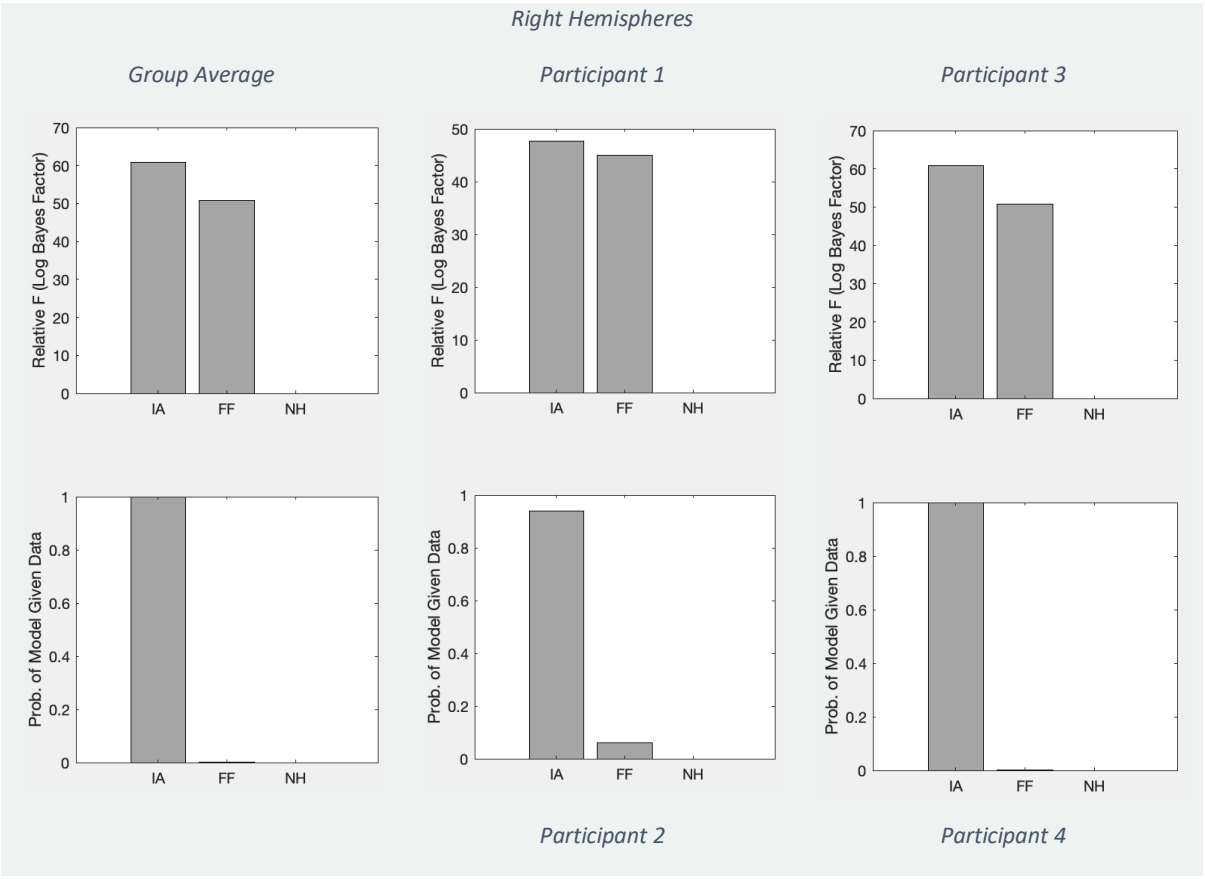
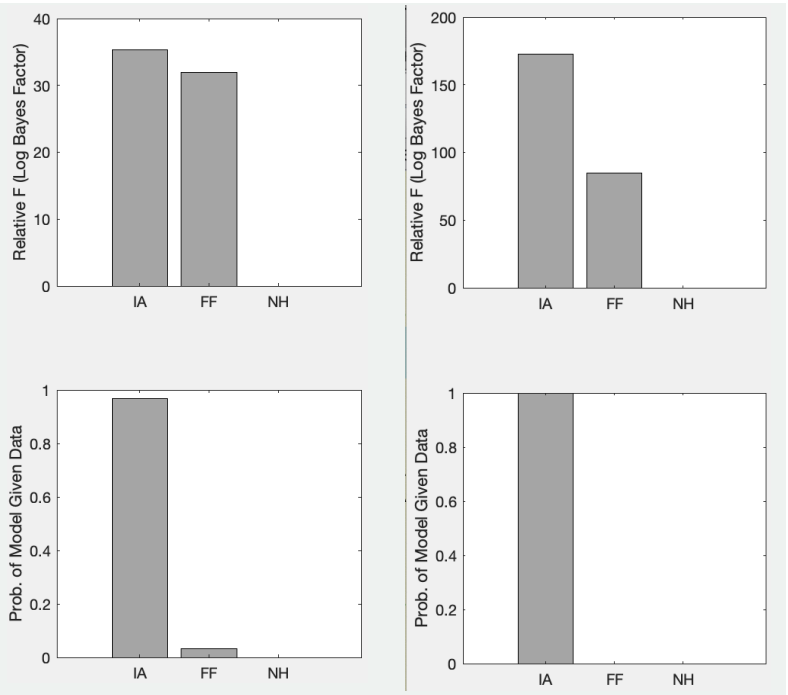



*Figure 47. Group and individual comparisons for right-hemisphere Interactive (IA), Feedforward (FF), and Null Hypothesis (NH) models.*




Consistent with bilateral group model results, both the unilateral group models showed strong evidence for nearly all of the feed-forward connections and also the presence of feedback connections. There were however, some differences. Firstly, both the left and right hemisphere lacked a forward connection between V1p and the ventral region. Secondly, the ventral region, in both the left and right hemisphere models, sent feedback connections to V1c and V1p. Neither of these feed-back connections were present in the bilateral model. Finally, the lateral dorsal to ventral connection was only present in the bilateral model.

In the unilateral group models nearly all the connections present in one hemisphere were also present in the other with the exception of: (i) dorsal feed-back connection to V1c, that was found only in the left hemisphere; (ii) dorsal feedback connection to V1p, that was found only in the right hemisphere; and (iii) ventral to connection to the dorsal region that was found only in the right hemisphere.

In both hemispheres, Bayesian model comparison once again showed that the IA model best explained the fMRI data. The strength of the evidence supporting this advantage, however, was considerably greater for the unilateral models than the bilateral model. In the left hemisphere, the group evidence for the IA model was 73.6 whereas it was 62.0 for the FF model, a difference of 11.6. For the right hemisphere, the group evidence for the IA model was 60.8 whereas it was 50.7 for the FF model, a difference of 10.1. Again, a difference of 10 or greater is considered very strong evidence in favour of the 'winning' model (Kass and Raftery 1995). Indeed, in both hemispheres the IA model had a probability of 100% compared to the FF model (0%) and the null hypothesis (0%). These results overwhelmingly support the presence of feed-back and lateral connections during reading.

## 4.4. Discussion

In this chapter, I tested the assumption that visual word recognition preferentially engages ventral structures by comparing how strongly three ventral stream areas (V4, VO1, and VO2) and three dorsal stream areas (V3a, V3b, and V7) responded during reading. Activity was also compared by task and condition to determine if those areas and streams are sensitive to the behavioural intentions of the participant or differences in the lexical, semantic, and phonological properties of the stimuli. Finally, the interactions between early visual (V1 central, V1 peripheral), dorsal, and ventral regions were estimated using DCM in order to determine whether processing across this network is better explained by a feedforward or interactive model.

The current findings demonstrate that contrary to the implicit assumption of most neurological models of reading, visual word recognition engages both ventral and dorsal visual areas even under normal reading conditions. Further, this dorsal involvement during reading is unlikely to be unidirectional with the DCM analysis showing strong feedback connections to the central region of V1 (and to a lesser extent, the peripheral region of V1). This result contrasts with classical neurological models of reading. When Dejerine (1892) reported a patient with a lesion to the left ventral occipito-temporal region, he explicitly assumed that the damaged grey matter was incidental to the patient's reading difficulties. He argued instead that the lesion severed the white matter linking the occipital lobes to the 'visual centre for words' located in the angular gyrus. In other words, visual information was being relayed through a ventral path to a dorsal region. More recently, neurological models consistently assume that visual information passes along the ventral stream to vOT where orthographic representations then form the input to the cortical reading system (Dehaene et al., 2005; Pugh et al., 2000). That is, only after information arrives in vOT is it spread to dorsal regions such as the inferior parietal lobule (Epelbaum et al., 2008). In contrast, the connection parameter weightings presented here suggest that during reading, interactions between and ventral areas are already taking place in the occipital lobe. The current findings contradict this conventional wisdom and show clearly that activation proceeds in parallel along both the ventral *and* dorsal streams.

The dorsal results may help to explain some inconsistencies in the pure alexia literature. For instance, although many patients with vOT lesions have acquired reading disorders such as pure alexia (Beversdorf et al., 1997; Binder & Mohr, 1992; Damasio & Damasio, 1983; Leff et

al., 2001) not all do (Ino et al., 2008; Philipose et al., 2007; Tsapkini, Vindiola, & Rapp, 2011). Moreover, not all patients with pure alexia have vOT lesions (Philipose et al, 2007). The most famous case studies of pure alexia were the two patients reported by Warrington and Shallice (1980) who had inferior parietal lobe damage that spared vOT. If visual information in V1-V3 separates into parallel streams targeting vOT on the one hand, and IPL on the other, then visual information about the stimulus might enter the cortical language system in multiple ways.

Independent evidence in support of this interpretation comes from Richardson and colleagues (2011) who conducted an fMRI study of reading in normal healthy adults and used dynamic causal modelling to evaluate the flow of information from visual cortex into the cortical language system. Their results demonstrated separable routes from V1, either ventrally through vOT or dorsally through the temporo-parietal junction. A follow-up study investigated a patient with extensive damage to left vOT who recovered some reading abilities (Seghier et al., 2012). The authors found that when he successfully read words it was due to information flowing from early visual cortices directly to the temporo-parietal junction without engaging vOT, suggesting that an intact dorsal stream can at least partially compensate for damage to vOT.

Another line of evidence highlighting dorsal stream contributions to reading comes from children with developmental dyslexia. By definition, these are children with normal intelligence who fail to attain the reading skill one would expect for their age, many of whom report visual difficulties when reading words. One prominent theory is that their reading difficulties are caused by abnormalities within the magnocellular visual system that

predominantly feeds into the dorsal visual stream (Stein & Walsh, 1997). Dyslexic children have been shown to have reduced contrast sensitivity at low spatial frequencies (Lovegrove, Bowling, Badcock, & Blackwood, 1980) and impaired motion sensitivity (Cornelissen, Richardson, Mason, Fowler, & Stein, 1995) relative to unimpaired readers of the same age. Moreover, Livingston and colleagues (1991) found that the magnocellular layers of the lateral geniculate nucleus were disordered in developmental dyslexics in post-mortem studies. Although it is clear that not all children with developmental dyslexia exhibit signs of magnocelluar dysfunction (Kronbichler, Hutzler, & Wimmer, 2002; Skottun, 2000), at least in some children abnormalities within the dorsal visual stream may contribute to difficulties learning to read.

It seems clear that the dorsal visual stream plays an important, if not well understood, role in normal reading. One hypothesis is that its primary contribution is to allocate spatial attention and help guide eye movements (Cohen et al., 2008; Pammer et al., 2006) but if so, it is unclear why activation levels varied depending on the nature of the stimulus (i.e. the main effect of condition). It is also unclear how the dorsal stream can compensate for damage to vOT in patients recovering from pure alexia (Seghier et al 2012). The current findings coupled with the small literature reviewed here imply a greater role than simple attention. Computational models of reading suggest that multiple paths from vision to meaning and sound play an important and complementary role in visual word recognition (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; Plaut, McClelland, Seidenberg, & Patterson, 1996; Zorzi, Houghton, & Butterworth, 1998). While it is unlikely that the ventral and dorsal visual streams map simply onto these different computational routes, the

underlying principle may hold: namely, that multiple pathways linking vision to sound and meaning are essential for skilled reading.

These pathways are very likely to be bidirectional. Across all comparisons performed in this experiment, the interactive model provided the best explanation for how effective connectivity changed during reading. This is perhaps unsurprising. Bi-directional models are more consistent with what is now known about the neuroanatomy of the primate visual system (see Kravitz et al., 2013) and bi-directional architectures are practically ubiquitous in computational models of reading.

# *5. Effects of Stimulus Timing on Early Visual Cortices*

## 5.1. Introduction

Previous chapters used four reading tasks to investigate visual contributions to word recognition. These tasks emphasized different aspects of the problem, focusing on either recognition (lexical decision), meaning (semantic decision), sound (phonological decision), or the more ecologically valid silent reading. Despite these differences, activation patterns were remarkably similar across early visual areas with the only task-based differences showing up in vOT, relatively high in the ventral visual stream hierarchy. A fifth task, a one-back working memory task that used written stimuli, was omitted from these analyses for two reasons. First, unlike the other four tasks, the one-back task is a working memory paradigm where the visual stimuli (words and non-words in this case) are essentially incidental. This contrasts with reading tasks where the stimuli are the primary focus of the experiment. Even so, one-back tasks are routinely used to functionally localize brain regions engaged by reading (Centanni et al., 2018; Diehl et al., 2014; Duncan et al., 2010; Szwed et al., 2011). There is a tacit assumption that occipito-temporal activations are driven by the orthographic stimulus and are essentially unaffected by the specific task. Previous studies have demonstrated that at least within vOT, this assumption does not hold; activation magnitude can change significantly for identical stimuli depending on the specific task demands (Mano et al., 2013; Yang & Zevin, 2014). This raises the second reason for omitting the one-back task from the previous analyses: namely, the pattern of activation for the one-back task was clearly different from the other four reading tasks, despite identical stimuli.

Figure 48 shows one participant's activation (words > rest) during covert reading (A) and during the one-back task (B). There is a noticeable difference in the pattern of activation across areas V1-V3. For covert reading, there is relatively stronger parafoveal/peripheral activation (yellow-red) coupled with de-activation (blue) in the most central region. Activation peaks during covert reading were consistently located in peripheral portions of V1-V3. In contrast, the same stimuli in the one-back task produced essentially opposite results. That is, the strongest activation was consistently located in the most central, foveal areas with de-activation present in the more peripheral regions. This general pattern of activity was found in all participants. Such a striking difference in not only the magnitude of the activation but also its spatial distribution has not been reported previously.

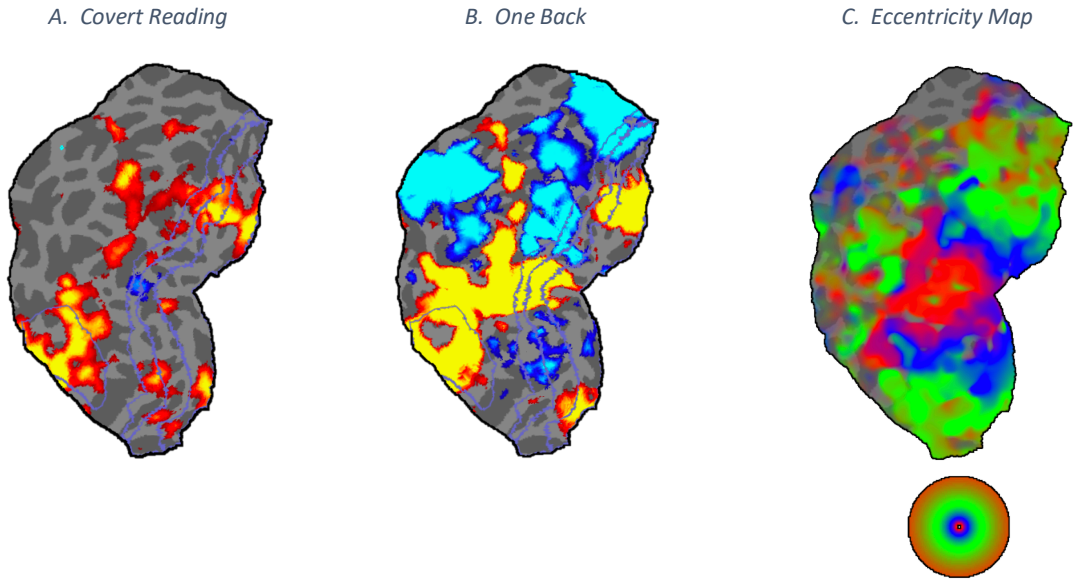



*Figure 48. One participant's activation (words > rest) for the covert reading (A) and one-back (B) tasks overlaid on their left occipital patch. (C) Eccentricity retinotopic maps also shown. In all participants, the one-back task more strongly engaged the most central, foveal region of V1-V3 with peripheral regions often showing strong de-activation. The covert reading task, in contrast, showed less activation in the most central region and instead had peak activity in parafoveal and peripheral coding regions.*

At a cognitive level, there are many differences between the covert reading and one-back tasks that could potentially explain this difference. Unlike the reading tasks, the one-back paradigm was designed to test visual memory (Owen et al., 2005) and was the only task in

the current investigation that could be successfully performed without reading the stimuli. It is possible that the lack of linguistic demands and the need to hold the previous stimulus in memory could be contributing factors in why the one-back task elicited such a noticeably different activation pattern. V1, for example, has been widely implicated in maintaining stimuli in visual memory during task (Bergmann, Genç, Kohler, Singer, & Pearson, 2016; Harrison & Tong, 2009; Serences, Ester, Vogel, & Awh, 2009). Even when the visual stimuli are identical, the V1 response can be different depending on whether the task requires making a judgement based on physical (e.g., colour) or conceptual (e.g., man-made) properties (Harel, Kravitz, & Baker, 2014). Without a much more comprehensive understanding of how different tasks are processed in the brain (Poldrack & Yarkoni, 2016; Price & Friston, 2005), it is very difficult to separate these types of effects from more general differences in attentional demand. Nonetheless, task-specific and attentional effects in the early visual areas suggest that these neural circuits are far more than just passive feature detectors and instead are involved in integrating bottom-up sensory signals with top-down factors including expectation and behavioural goals.

At a more prosaic level, the reading tasks and the one-back task also varied along several dimensions: the one-back task used a fixed, rather than jittered, interstimulus interval (ISI); stimuli in the one-back task were shown at a much faster rate than in the other tasks; and the one-back paradigm used a blocked design while the reading tasks were primarily event related. In the one-back task, stimuli were presented one per second with a fixed inter-stimulus interval. Moreover, they were blocked so that 16 trials in a row all came from the same category of stimuli (e.g. all pseudowords or all high frequency words). Because the behavioural response did not depend on the nature of the stimulus (just whether or not it

repeated), this made the task much more efficient (Dale, 1999) and allowed for a shorter run of data acquisition (4:18 [min:sec] vs 12:08 runs for one-back vs. covert reading, respectively).

Changing the presentation rate during a reading task can have a measureable effect on the neural response in occipital and occipitotemporal regions with rate increases (from 20, 40, to 60 words per minute) shown to have a positive linear effect in both fMRI (Mechelli, Friston, & Price, 2000) and PET (Price, Moore, & Frackowiak, 1996). In retinotopically defined V1-V3, increasing stimuli rate from 1hz to 4hz doubled response amplitude in those regions (Mukamel, Harel, Hendler, & Malach, 2004), although in this case object stimuli (houses and faces) were used rather than words. Interestingly, the linear relationship they found between stimuli rate and activation was not constant across the different stages of the visual hierarchy and the 200% increase they found in the early visual areas was accompanied by only a 25% increase in occipitotemporal cortices. Importantly, and in contrast to the present results, the voxels that were more active during the fast (4 Hz) condition were a subset of the voxels activate in the slow (1Hz) condition, suggesting that the rate change primarily impacted the *amplitude* and not the overall spatial *pattern* of activation. In contrast, in the current study, the fast task (i.e. one-back) produced a conspicuously different activation pattern than the slow tasks (e.g. covert reading).

In other words, there are several possibilities for why the one-back task was exceptional relative to the other four reading tasks. The objective of this chapter was to explore how the response of the visual areas is affected when high-level requirements of those tasks are held constant and their low-level paradigm properties (e.g. stimuli rate) are swapped.

Participants performed two modified versions of the original covert reading and one-back tasks. The 'fast' covert reading task used the faster timings from the original one-back task and the 'slow' one-back task used the slower timings of the original covert reading task. The resulting activation patterns from this rate manipulation were then compared with activation patterns from the first experiment to see if the differences were due to the changing task or to the changing presentation parameters. The two different hypotheses make very clear predictions:

1. If task is driving the activation patterns, then the specific timing parameters will be irrelevant and one would expect to observe the same pattern of results as the original experiments. If so, this suggests that it is the specific cognitive factors when performing each task that drive the activation patterns in early visual cortices.

2. If the stimulation parameters are driving the activation patterns, then one would expect to observe a cross-over where the original one-back will look like the new covert task because they share the same timing characteristics, even though the tasks are different. Similarly, the original covert reading results will look like new one-back results for the same reasons. If so, this implies that the specific presentation parameters have a much larger influence on the pattern of results than is typically appreciated in the literature.

## 5.2. Methods

The same participants who performed the original experiment returned for an additional testing session where they each performed the two modified tasks in the scanner: the slow one-back and the fast covert reading task. The primary difference between the modified tasks and their original forms was the timing of the stimuli. Specifically, the slow one-back task was slowed down by using the same ISI as the original covert reading task (jittered ISI of 2500-5500ms). Because that ISI was used in a mixed blocked-event related design, this meant fewer trials per block. It also allowed me to randomly inter-mix trials from different conditions and analyse them in an event-related fashion. In other words, the slow one-back task was conducted exactly as the original covert reading task was performed. In addition, the fast covert reading task was sped up by using the same ISI as the original one-back task (fixed ISI of 1000ms). Because covert reading was the only reading task not to require an overt response, running it at this faster rate was fine. It did require, however, blocking the stimuli so that all the items in a block came from the same stimulus category (i.e. low frequency words, high frequency words, pseudowords, or consonant letter strings) because there was insufficient time between trials to distinguish individual events (Dale, 1999; Josephs & Henson, 1999). Each task was done only once with participants completing both tasks in a single scanning session. As before, the fMRI data from each task were overlaid on the participant's flattened occipital patch along with the retinotopically defined V1-V3 ROIs.

## 5.3. Results

As can be seen in Figure 49, the activation patterns for the rate-modified versions of the covert reading and one-back tasks are noticeably different from the original tasks. For covert reading, increasing the stimulus rate had two fairly consistent effects on neural activity. First, in all participants, there was increased activation within foveal coding regions in V1-V3 and beyond. Typically, this included a strong response in voxels not significantly active in the original, slower version of the task. Second, there was decreased activation (or increased de-activation) within peripheral coding regions. Altogether, the activation pattern for rapid covert reading looked much more like the original one-back task than the original covert reading task. Slowing down the one-back task to the speed of the original covert task had a complementary effect on activation. Compared to the original task, activation decreased in foveal coding regions and increased in peripheral regions resulting in an overall activation pattern that much more closely resembled the original covert reading task than the original one-back task. In other words, the new patterns of activation were entirely consistent with the second hypothesis, namely that stimulation parameters, rather than task demands, drove the change in activation in early visual cortices.

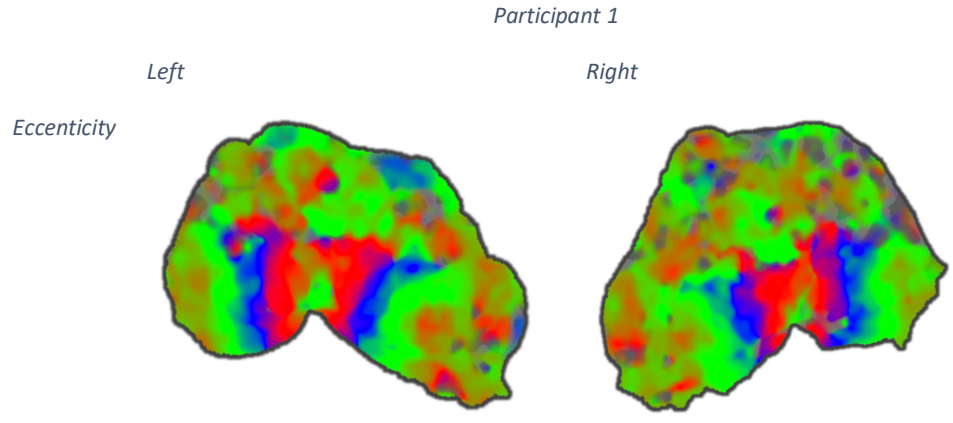
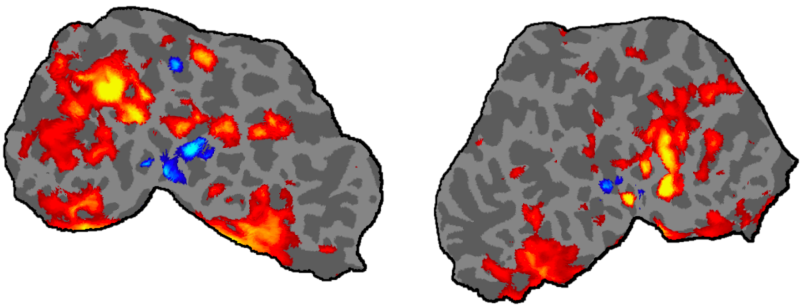


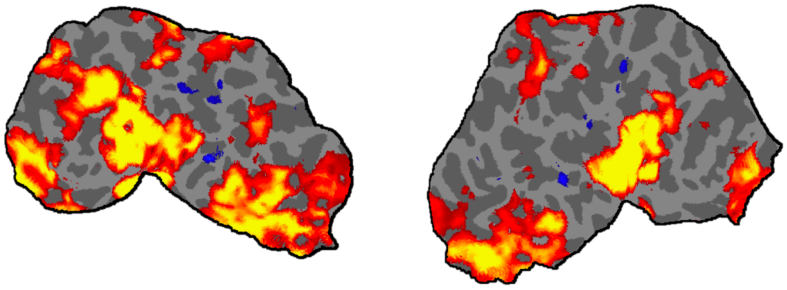

*Figure 49. Activation (words > rest) for the covert reading (original and fast version) and one-back (original and slow version) tasks overlaid on each participant's left and right*

*Covert*

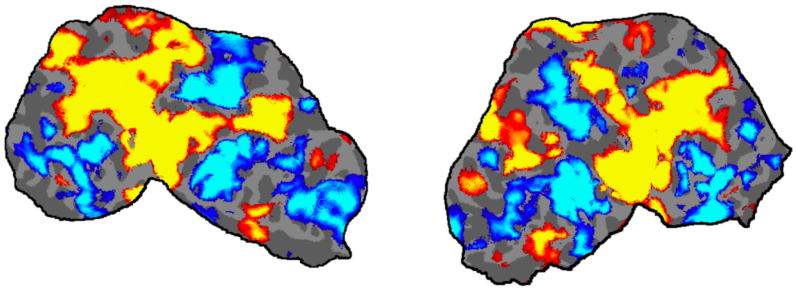


*hemisphere occipital patches.*

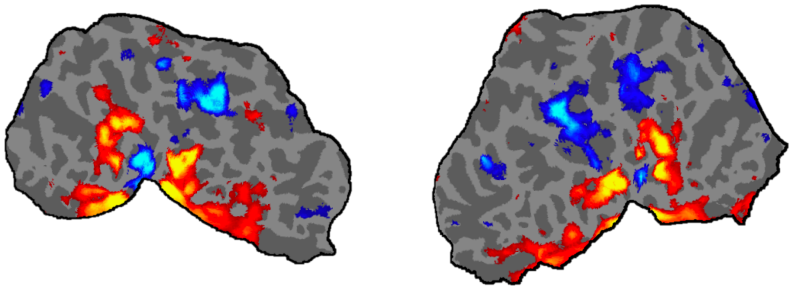
*Covert (fast)*



*Oneback*



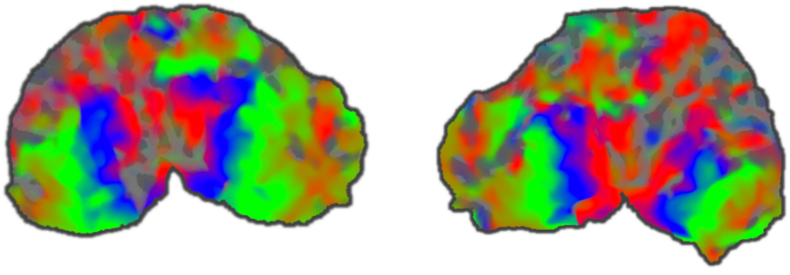
*Oneback (slow)*



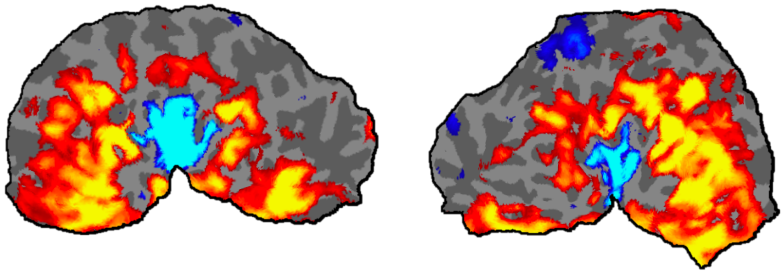
*Participant HC*

*Left* *Right*

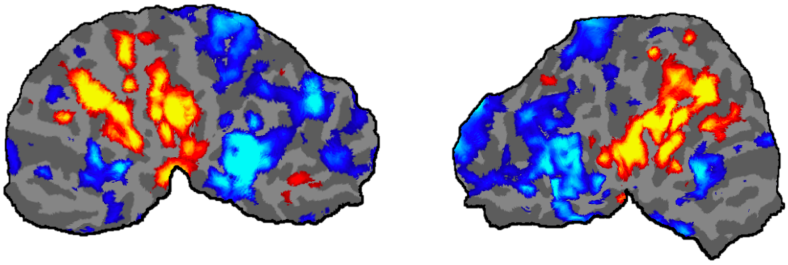
*Eccenticity*



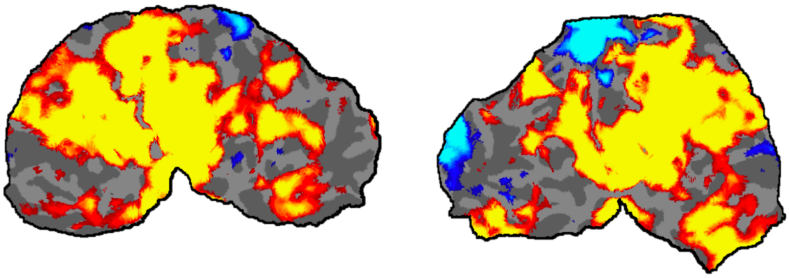
*Covert*



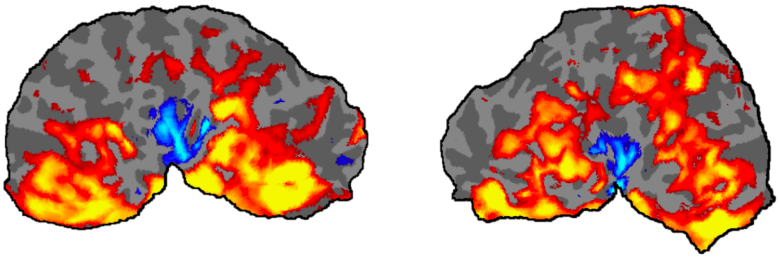
*Covert (fast)*



*Oneback*



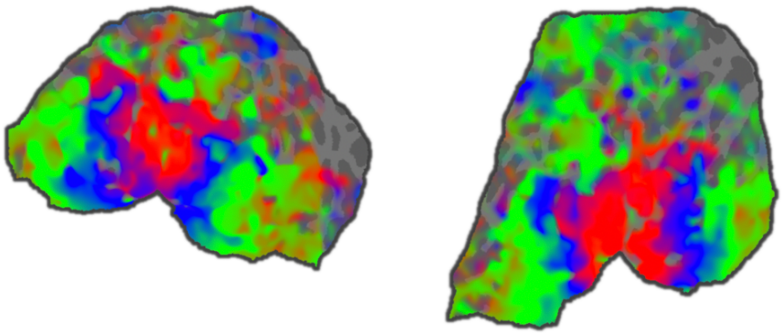
*Oneback (slow*



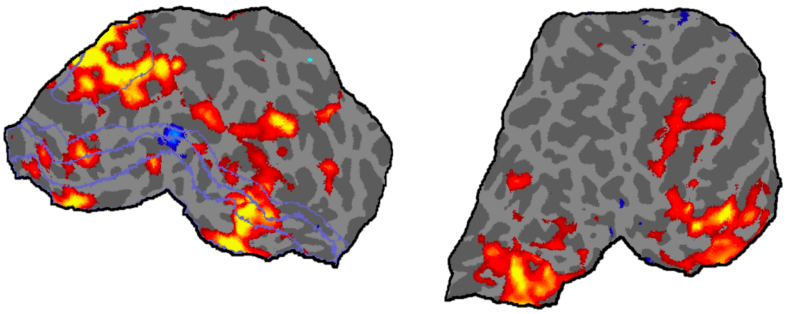
*Participant 3*

*Left* *Right*

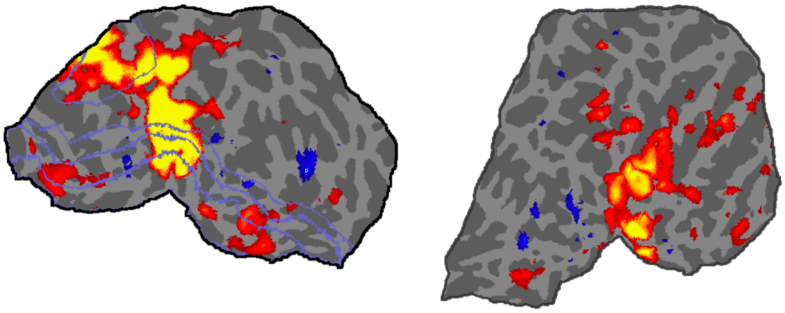
*Eccenticity*



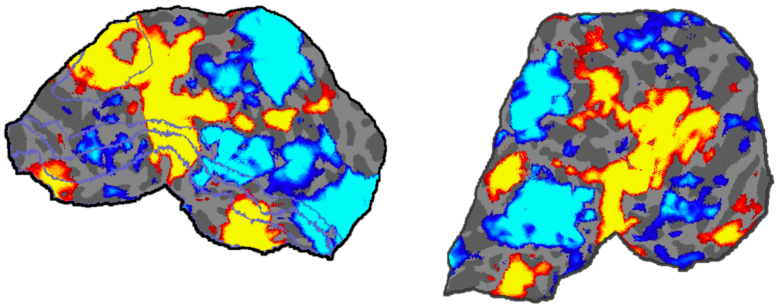
*Covert*



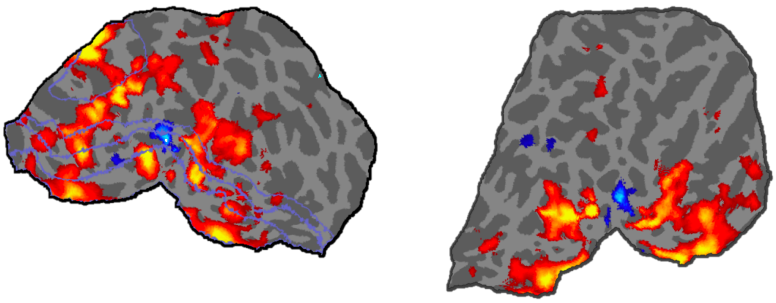
*Covert (fast)*



*Oneback*



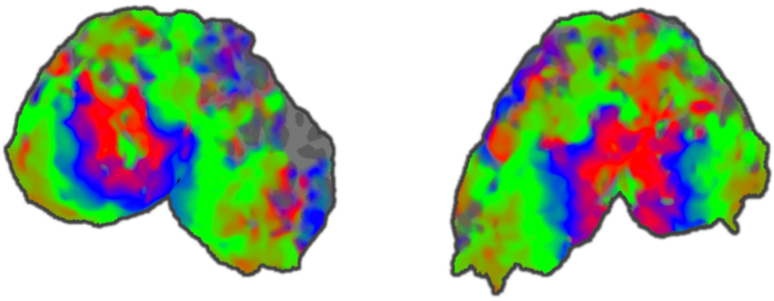
*Oneback (slow*



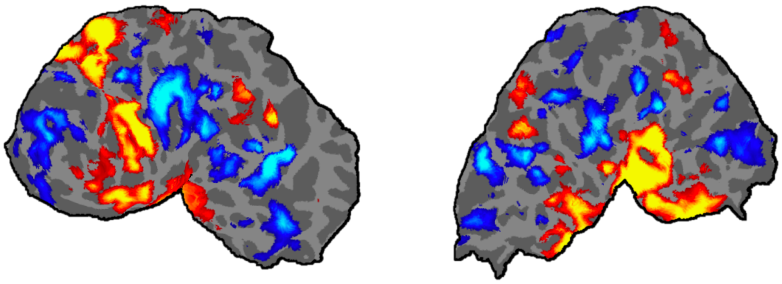
*Participant 4*

*Left* *Right*

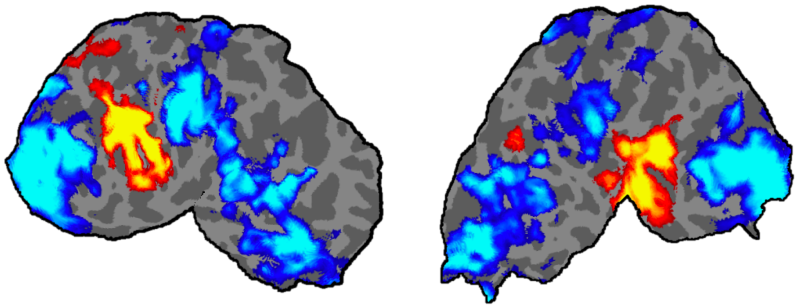
*Eccenticity*



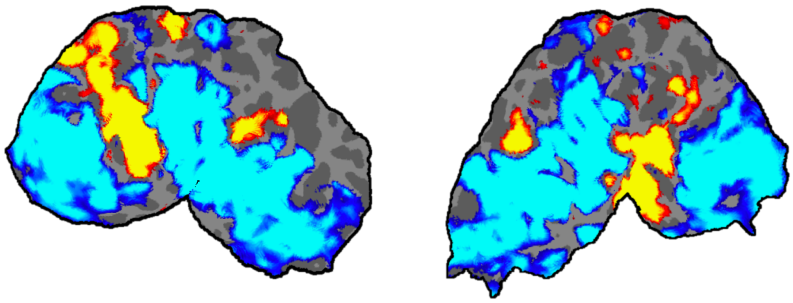
*Covert*



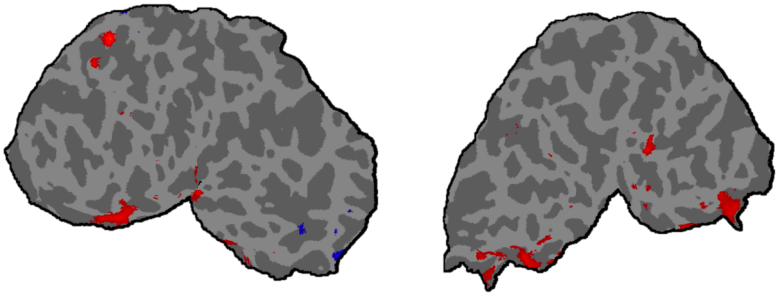
*Covert (fast)*



*Oneback*



*Oneback (slow*



## 5.4. Discussion

This experiment investigated why the one-back task elicited such a noticeably different pattern of activation than the other four reading tasks. Specifically, it explored whether the difference was due to intrinsic task differences or whether it was due to the role of stimulus rate. In other words, all other things being equal, could a low-level property of the experimental design such as the rate of present account for the difference in neural response? Swapping the stimulus timings between the original covert reading and one-back tasks dramatically changed the activation pattern of two tasks. Those with rapid presentations (i.e. the original one-back and the new, fast covert reading) looked highly similar while those with two slow presentations (i.e. the original covert reading and the new, slow one-back) looked highly similar, suggesting that stimulus rate was a driving factor in the different activation patterns and not the high-level task requirements. This finding that high-level task demands were not the predominant factor in the original one-back's unusual activation pattern is consistent with the results from the previous chapters where task differences did not emerge until vOT.

Interestingly, changes to the stimulus rate did not simply scale the response within the regions already engaged in the original task but produced a noticeably different pattern of activation. For example, in most cases, increasing stimulus rate both activated previously de-active populations (predominantly in foveal regions) and de-activated previously activate populations (predominantly in the periphery).

Spatial attention is one factor that can strongly influence activation in the early retinotopic cortices. The paradigmatic example is where covertly attending to a location in the visual field enhances activity in a retinotopically specific manner in the extrastriate (Brefczynski & DeYoe, 1999; Gandhi, Heeger, & Boynton, 1999; Ress, Backus, & Heeger, 2000; Somers, Dale, Seiffert, & Tootell, 1999; Tootell et al., 1998) and striate cortices (Brefczynski & DeYoe, 1999; Gandhi et al., 1999; Kastner, Pinsk, De Weerd, Desimone, & Ungerleider, 1999; Martinez et al., 1999; Somers et al., 1999; Tootell et al., 1998). The allocation of spatial attention has also been found to de-activate retinotopic cortices coding for regions outside the point in the visual field being focused on (Tootell et al., 1998) suggesting that attention may operate in a push-pull manner. One possible interpretation of the current results is that the faster stimulus rate increased attentional demand, presumably to the foveal region of the visual field where the stimuli appeared, leading to greater activation in foveal coding regions along with decreased activation (or increased de-activation) in the surrounding peripheral coding regions. The general finding that regardless of tasks, a faster stimuli rate elicits stronger activation in foveal coding regions and weaker activation in peripheral coding regions is consistent with 'spotlight' models of attention (Brefczynski & DeYoe, 1999) and those positing a push-pull effect of allocating attentional resources to specific spatial locations (Tootell et al., 1998).

The stimuli rate effects also had a noticeable impact on activation in areas beyond V1-V3 with dorsal lateral (up to and including V5) and ventral lateral (up to and including vOT) regions responding to the change. A repeated finding in the human neuroimaging literature (e.g. Kastner, De Weerd, Desimone, & Ungerleider, 1998; Kastner & Pinsk, 2004; Martinez et al., 1999) is that, in general, spatial attention effects tend to be stronger in higher visual

areas. Attention might first modulate activity in extra-striate areas before being fed back to earlier areas such as V1 (Lamme & Roelfsema, 2000; Martinez et al., 1999; Noesselt et al., 2002)

In other words, changing the rate of stimulus presentation had a profound effect on the pattern of activation observed in early visual cortices, which has two important implications. First, it demonstrates the importance of the specific paradigm parameters in reading experiments. These may be especially important for investigations of early visual cortices, but it's clear they affect higher order areas such as vOT as well (Mechelli et al., 2000; Price, Moore, et al., 1996). Second, it is a clear indication that the activation is not stimulus-bound. That is to say, these are not reading-specific activations because the stimuli were exactly the same across the two versions of each task. This is yet another finding inconsistent with the notion of reading-specific neuronal representations (Price & Devlin, 2003, 2004).

# *6. General Discussion*

The aim of this thesis was to investigate whether the visual cortices contribute to reading beyond simply conveying visual information from the retina into the cortical language system. A prominent neurological model of reading explicitly assumes that written words are recognized via a set of feedforward steps through the ventral visual pathway that aggregate low level visual information into features and then letters, bigrams, and finally visual word forms that provide the input to the brain's reading network (Dehaene et al., 2005). The process of learning to read causes neurons to be "recycled" such that their receptive fields become tuned to orthographic patterns and thus respond specifically to written stimuli (Dehaene & Cohen, 2007). This account, however, stands in contrast to modern conceptions of the highly dynamic and flexible processing carried out in the visual cortex where information flows in both a bottom-up and top-down fashion through multiple parallel streams, with neuronal representations changing dramatically depending on the specific processing demands (Gross, 2010; Kravitz et al., 2013). As a result, the work presented here set out to systematically test whether visual processing during reading was influenced by non-visual factors such as the specific task being performed or higher-order lexical properties of the written stimulus. There were several notable findings:

- Reading engages not only the regions of V1-V3 that receive input from central region of the retina that covers the fovea and parafovea – that is, where the words physically appeared – but also regions coding the periphery, far outside the expected retinal extent of the stimuli. Peripheral activation was consistent across all four reading tasks but its specific contributions remain unclear. Auditory association projections to early visual areas are strongest to the periphery suggesting that these

activations could potentially play some role in audio-visual integration, an important aspect of reading.

- Reading activates not only ventral visual areas (V4, VO-1, VO-2) but also dorsal regions (V3a, V3b, V7), with no evidence of any difference in the magnitude of activation between them. Moreover, activity in both sets of regions was influenced by stimuli condition (i.e. low frequency word, high frequency word, pseudoword, or consonant letter string). Although the differences between individual conditions did not reach significance, it was noteworthy that the pattern was consistent across all the areas and matched that observed in vOT, where low frequency words were significantly more active than high frequency words. Neither of the two neurological models of reading provide much guidance for interpreting these findings.

- Effective connectivity analyses overwhelmingly support the presence of feed-back connections, in addition to the uncontroversial feed-forward connections. These were present in both the ventral and dorsal visual pathways, with lateral connections linking the two. Moreover, there was no evidence of different connectivity profiles between the left and right hemispheres.

- Stimulation parameters that are typically considered incidental such as stimulus presentation rate can have dramatic effects on neural activity in V1-V3 during reading. Faster stimuli rates produced stronger central and weaker peripheral activation while slower rates produced weaker central and stronger peripheral activation. These results contradict the notion of reading-specific neuronal representations within the visual cortices because the stimuli were identical across

both versions of the experiment. This finding highlights the importance of seemingly irrelevant experiment details for future investigations of early visual contributions to reading.

- Finally, there were virtually no significant differences observed across analyses between the left and the right hemisphere. The only exception was in vOT where activation was significantly greater in the left relative to the right hemisphere. This finding is consistent with Cohen et al. (2002) who reported bilateral activation of early visual areas up to, but not including, vOT. In both cases, the difference was quantitative rather than qualitative. That is, reading produced activation in both left *and right* vOT, although the activation was stronger in the left hemisphere.

These findings demonstrate that the early visual cortices play a much more complicated role in reading than simply aggregating visual features into orthographic representations. The results suggest that top-down modulations play a significant role in early visual processing during reading, although the nature of this role remains unclear. Similarly, it seems obvious that both the ventral *and dorsal* visual streams contribute to visual word recognition but the nature of these contributions is uncertain. In other words, the current results represent an important first step towards recognizing the contributions that the early visual cortices make during reading, but they also raise additional questions.

## 6.1. Limitations

It is also important to recognize methodological limitations of the work that limit the implications that can be drawn from these findings. First, I opted to intensely study a small group of participants (n=4) in a multi-case study approach rather than test a larger sample size using a more typical group study (n≈30) as is common in neuroimaging studies of reading. This decision was motivated by a need to functionally map retinotopy in each participant in order to precisely and accurately identify individual visual fields. Even so, the small sample size introduces statistical sensitivity issues (Button et al., 2013). Small sample sizes are associated with low statistical power, increased false positives, inflated effect size estimation, and low reproducibility. In other words, a larger sample would offer much greater statistical sensitivity which could potentially help to reveal which condition differences were driving the main effect of stimuli seen in both ventral and dorsal visual areas. On the other hand, a larger sample might reveal that the apparent differences were in fact overestimates resulting in a false positive in those regions. Without additional data it is impossible to know which, if either, of those possibilities is correct. The problem arises, however, in determining what is a sufficient number of participants for detecting true effects. A recent paper by Lorca-Puls et al. (2018) reported that even reasonably large (n=30-90) samples of stroke patients can produce highly inconsistent lesion-deficit results. Only when the same became very large (n>150) did the results begin to stabilize. For the experiments reported here, testing a sufficiently large sample (n≈30-150) was impractical which means that it will be important for subsequent studies to attempt to replicate the findings.

The small number of participants meant that combining them into a group analysis had limited sensitivity. In Chapters 3-5, group analyses were conducted to summarize the data and illustrate overall trends, but the main results were presented in individuals. Because each participant completed a large number of reading trials (2830 trials collected over 25 task runs), statistical sensitivity may have been limited by the standard multi-level linear modelling I used here (Beckmann, Jenkinson, & Smith, 2003). The recent advent of linear mixed modelling analyses for fMRI (Chen, Saad, Britton, Pine, & Cox, 2013) allows for more flexible modelling of variance-covariance structure in the data and would be expected to increase sensitivity in the small, but deep, data sets collected here. Nonparametric (Nichols & Holmes, 2002) and Bayesian inference (Congdon, 2006; Zhang et al., 2007) analysis methods also have advantages for experimental designs with low degrees of freedom. In other words, the summary analyses conducted on the group data may have benefited from non-traditional fMRI analysis methods that make fewer assumptions about variance structure and therefore are potentially more sensitive for small N studies.

It is worth noting that all of the first level fMRI analyses in the thesis (both those conducted in FSL and the those used in the DCM analyses conducted in SPM) relied on a common 'canonical' model of the HRF (Glover, 1999). Although unbiased, the Glover model is inflexible and does not account for variability in the shape and timing of the haemodynamic response across voxels (Birn, Saad, & Bandettini, 2001; Handwerker, Ollinger, & D'Esposito, 2004) thus limiting statistical sensitivity. The use of basis sets (Friston et al., 1998; Woolrich, Behrens, & Smith, 2004) or non-linear models (Buxton et al., 1996) offer significant improvements in sensitivity although the first-level fMRI results cannot easily be combined into participant-level or group-level analyses. Given the large number of independent runs

for each participant (n=25), it was essential to choose an analysis method that allowed these to be combined into participant-specific results, even if this resulted in a potential loss of sensitivity.

A more fundamental limitation is the process of delineating neural populations to include in the analyses. In this thesis, brain activity was analysed in a two-step process. First, I created a binary mask that included all voxels within an ROI exceeding the activation threshold (Z=2.3). Second, I calculated the mean activation across all the voxels included in that mask. This thresholded masking approach is common in fMRI studies of reading and was selected, in part, to make my results easier to compare with the key studies underpinning the LCD and IA models. Unlike those previous studies, however, I used accurate retinotopic maps to define my ROIs and so limiting the analysis to only supra-threshold voxels may not have been the best approach for answering my experimental questions. After all, the regional boundaries drawn according visual field maps reflect important functional, cytoarchitectural, and connectivity differences in the early visual cortices (see General Introduction). If these maps delineate functional units (Zeki, 1993), it may be more informative to analyse neural activity across the entire region rather than just by selecting a subset of voxels exceeding an arbitrary threshold. For example, in the early visual cortices, spatial attention can manifest in a push-pull manner with increased activation in the attended location and decreased activation outside of it (Tootell et al., 1998). In such a system, the relative differences in sub-threshold activation (including deactivation) across the region may provide useful information on how effective top-down inputs are (in this example, suppressing task irrelevant retinotopic regions). Analysing the neural response across a region may better capture both the faciliatory and inhibitory effects of feedback

and avoid the need to set arbitrary thresholds on what voxels to include and exclude. Calculating effect size in this way could improve the sensitivity to spot top-down influences and could dramatically impact results. Indeed, when I analysed neural activity across *all* the voxels in the central region of V1, low frequency words elicited a significantly higher activation than low frequency words (see Appendix B).

Another practical limitation of the current work was that the scanning was carried out on a 1.5T MRI scanner. Lower field strength scanners offer excellent reliability and consistency but are limited in their spatial resolution. High field MRI such as modern 7T scanners offer considerably increased signal-to-noise (Uğurbil, 2018) and less spatial aliasing due to draining veins (Turner, 2002) allowing laminar-level spatial resolution. Within mammalian isocortex, feedforward projections target the granular layer and originate predominantly in the supragranular layers while feedback connections do not target the granule layer and originate predominantly in the infragranule layers (Felleman & Van Essen, 1991; Markov et al., 2014). In other words, 7T MRI offers the spatial resolution to potentially distinguish between bottom-up and top-down information flow that would more directly assess the claims made by different neurological models of reading (Dehaene & Cohen, 2011; Price & Devlin, 2011).

Despite its excellent spatial resolution, the temporal resolution of functional MRI is intrinsically limited by the haemodynamic response which is very slow (i.e. seconds). In contrast, magnetoencephalography (MEG) directly measures changing magnetic fields due to electro-chemical activity in populations of neurons and thus has an intrinsic temporal resolution on the order of milliseconds. As a result, MEG is excellent at detecting the

frequency synchronization between areas that has been proposed as a mechanism of effective interareal communication (Fries, 2005; Fries, 2015). There is evidence that the gamma-frequency band might mediate feedforward influences (supragranular layers show local gamma-band synchronization) and alpha-beta frequency band might mediate feedback influences (infragranular layers show local alpha/beta-band synchronization) with cognitive tasks that require stronger top-down control generating comparatively greater alpha-beta activity (Bastos et al., 2015a). Attention may rely on alpha-beta synchronisation with alpha and beta bands potentially playing differential roles (see Fries, 2015 for a recent discussion). In other words, MEG also offers the potential to more clearly distinguish bottom-up from top-down interactions during reading in order to better understand their differential contributions. Ultimately, any comprehensive understanding of reading at a neuronal level will require far better spatial and temporal resolution than was available to me when collecting the data in this thesis.

## 6.2. Implications & future directions

It seems clear that none of the existing neurological models of reading area entirely consistent with current results nor do they provide adequate explanations for some of the novel findings. For instance, what are the specific contributions from the peripheral visual fields during reading and why do they change so dramatically when the stimulation parameters are altered? Do the dorsal stream regions contribute solely to spatial attention and eye movements during reading or do they also contribute to visual word recognition? Are the top-down interactions best understood in a predictive coding framework, as attentional modulation, as audio-visual integration, or as some combination of these

factors? At a minimum, both the LCD and interactive model would need extensive modification to begin to address these questions, although a new model may prove more expedient.

A more satisfactory model would need to account not only for how bottom-up visual information flows through, and is transformed by, these early dorsal and ventral structures but also how the wider cortical language network interacts over time to recognise words. Understanding and describing the temporal dynamics of this system requires a more comprehensive model of both the critical structures involved in reading and the neuroanatomical connections linking them together. Currently, the critical cortical network for reading includes, at a minimum, two frontoparietal circuits and the vOT (see Figure 50). How those reading related structures are connected and interact over time, however, is not adequately understood. Although, recent connectivity studies are providing an increasing detailed picture of their major neuroanatomical inputs and outputs (Lerma-Usabiaga, Carreiras, & Paz-Alonso, 2018; Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012; Yeatman et al., 2013). How ascending visual information reaches this cortical reading system is also not entirely understood but likely involves, as this thesis suggests, numerous pathways rather than the single ventral route assumed by classical (Dejerine, 1892) and neo-classical neuroanatomical models (Dehaene et al., 2005).

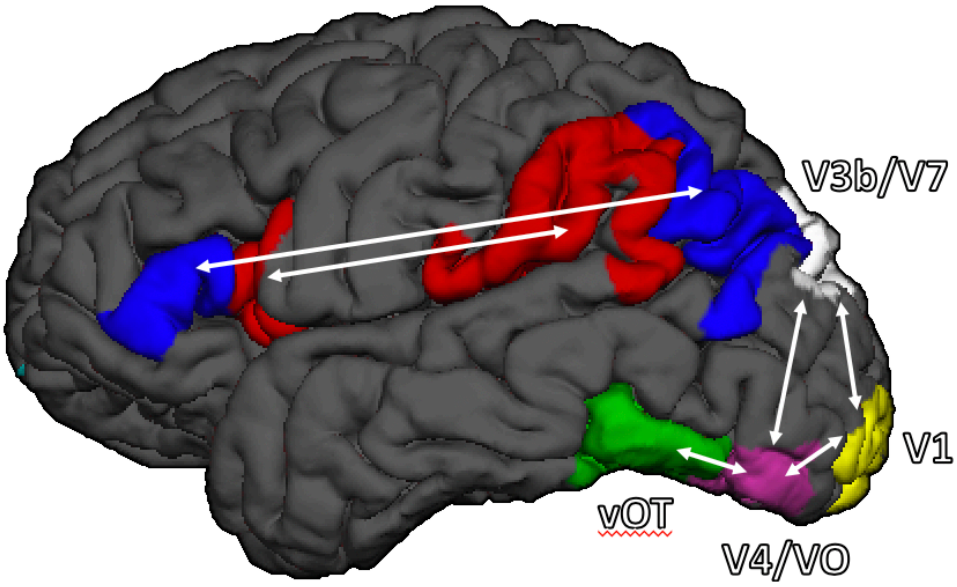



*Figure 50. Cortical reading network including the fronto-parietal circuits (red and blue) and the vOT (green) shown on participant #3's left hemisphere. The fronto-parietal circuits include (i) posterior parts of Broca's area and the supramarginal gyrus, both shown in red, that preferentially contribute to phonological processing and (ii) the more anterior and ventral parts of Broca's area and the angular gyrus, both shown in blue, that preferentially contribute to semantic processing (see section 1.2 for more information). The vOT, shown in green, is involved in the visual processing words (see sections 1.3 and 1.4 for more information). Also shown are V1 (yellow) and the dorsal (white) and ventral (purple) regions included in the DCM analyses (see Chapter 4). Results from that analysis suggest that, during reading, there is a bidirectional flow of activity between V1 and dorsal and ventral regions.*

At a computational level, visual word recognition is one of the most well studied behaviours in cognitive science (Coltheart et al., 2001; Plaut et al., 1996; Seidenberg & McClelland, 1989; Zorzi et al., 1998). Despite the considerable differences between the computational models, these efforts have identified a common set of principles that appear to be critical for reading including multiple routes from orthography to phonology and semantics and interactivity between these components. All of the models, however, assume that the input to the system is some form of dedicated orthographic code and in light of the current findings, this assumption becomes suspect. It seems clear that information processing that is important for reading is happening within the visual cortices, long before any orthographic representation is extracted (if, indeed, reading-specific representations are ever extracted). As a result, 'orthographic inputs' to reading models need to be re-

conceived as dynamic visual components that include, at a minimum, separable ventral and dorsal input streams with multiple layers of feature extraction and top-down modulation from higher order areas.

With such models in hand, it will be possible to explicitly test competing accounts by implementing specific hypotheses in the model, observing its behaviour and testing whether it correctly predicts human reading behaviour. For instance, competing hypotheses about the role of attention vs. predictive coding can be easily implemented in the model to generate testable predictions for future *in vivo* experiments. Similarly, damage to the model can be used to test its adequacy when predicting acquired lesion-deficits and/or developmental disorders such as dyslexia that follow from abnormalities in specific components. If the work presented here helps to motivate a new generation of neurobiologically-inspired computational models of visual word recognition, then it will have achieved neuro-scientific impact by highlighting the importance of visual cortex contributions to reading and by extending our understanding of the interactions between vision and language. In addition, such models offer the potential for real-world impact by providing i) novel insights into the relation between structural abnormalities and development reading disorders; ii) the ability to accurately predict the consequences of strokes on reading ability; and iii) a testing platform for evaluating intervention strategies for helping to ameliorate developmental or acquired reading impairments.

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# Appendix A

## 1. Japanese study

### 1.1. Introduction

As described in Chapter 3, the four reading tasks strongly activated not only the central foveal and parafoveal regions of V1/V2/V3 but also regions mapped to the far periphery (>10° visual angle), well outside the expected retinotopic extent of stimuli. In all tasks, the stimuli were presented centrally (at the point of fixation) and had a maximum width of 3.0° visual angle or less. Nonetheless, the participants showed strong activation outside the central ROI (≤3.4°), often in regions mapped to 10° visual angle and beyond. This is a considerable distance from the stimulated central region, especially in the tightly bound retinotopy of V1. Indeed, the distance is too far to be mediated entirely by horizontal connections; they are weak acting (being modulatory rather than driving), slow conducting, and cover too little of the visual field to elicit such a strong response that far from the stimulated central region (Angelucci & Bullier, 2003). Another possibility is that the peripheral activation resulted from unforeseen light contamination during scanning such as the projector illuminating regions of the scanner bore not just the presentation screen. If so, the light contamination would be present for both the orthographic stimuli and the plain fixation cross (i.e. baseline) conditions and therefore would be expected to subtract away when contrasting stimuli to fixation. Light artefacts aside, the strong peripheral response could also be the result of feedback activity. One hypothesis, albeit speculative, is that the peripheral activation is somehow related to the linguistic associations of the stimuli. This hypothesis could not be adequately tested using the data collected in Chapter 3 as the

pseudowords, although meaningless, had phonological associations and the consonant strings, that were both unpronounceable and meaningless, were presented in tasks where the participants were asked to say 'ok' silently whenever they saw one. A better approach for testing the hypothesis required introducing a new stimuli condition, one that was comparable with the original letter string stimuli in terms of spatial features and visual complexity but that lacked any phonological or semantic associations. I achieved this by using Katakana, a Japanese alphabetic script, to create a stimulus set of 4-5 letter words in Japanese. Because none of the participants spoke, let alone read, any Japanese, these stimuli had no phonological or semantic associations. The aim of the experiment was to compare participants' neural activity during the covert reading of English words with covert 'reading' (i.e. passive viewing) of Katakana words, to test the hypothesis that peripheral activation in V1 was due to top-down, higher-order associations. If so, then covert reading of English relative to Japanese (Katakana) words would be expected to reveal significant peripheral activation in V1. In contrast, if the peripheral activation were due to a different factor such as contamination from the projector stimulating the periphery, then no difference would be expected.

## 1.2. Methods

Three of the four participants from Chapter 3 performed five runs of the modified covert reading task where the consonant string and pseudoword blocks were replaced with blocks Katakana strings (for full stimuli set, see Appendix C, section 2). As in the original covert reading task, there were still 120 trials presented in 12 blocks of 10 items each and all the

timing parameters remained the same (total run time of 12:08mins). In the modified version however, the 30 consonant string and 30 pseudoword trials were replaced by 60 Katakana stimuli. There were five runs of the modified covert reading tasks for a total of 300 Katakana stimuli (60 Katakana per task run × 5 runs). The same 150 low frequency words and 150 high frequency words from the original covert reading task were used again. Blocks alternated between Katakana and English such that an English block always followed a Katakana block or vice versa. Three of the five tasks started with a Katakana block, the other two started with English.

The same scanning, image processing, and analysis procedure was also used. There were three planned contrasts: (i) Katakana > rest; (ii) English > rest; and (iii) English > Katakana.

## 1.3. Results

The initial analysis focused on replicating the basic activation patterns seen in Chapter 3 for English words relative to rest (Figure 47). In one participant (#3), the activation was similar with activation present in both central and peripheral regions of V1-V3 as well as in vOT, bilaterally. The other two, however, showed considerably less activation than anticipated. Participant #1 had almost no activation in V1-V3 or in vOT while Participant #4 showed only minimal activation in V3 and vOT but none in V1-V2. The cause of this unusual data was unclear; visual stimulation versus fixation would certainly be expected to produce early visual activity. To test this, two additional analyses were conducted comparing i) the Katakana stimuli to fixation and ii) all stimuli (English and Katakana) to fixation. The results

were essentially unchanged. The one participant who showed robust activation for English words also showed robust activation for the other two comparisons whereas the other two participants showed little-to-no early visual field activation for Katakana or for all stimuli relative to fixation.

Normally, when a basic contrast like [visual stimuli > rest] fails to show activation in visual cortices, it is the result of a timing error in the data analyses; that is, it is due to mis-specifying the model. In this case, the timings were identical to those used in the original analyses (only the stimuli had changed) and a direct comparison confirmed that the model timings were identical. Even so, a shift in the volumes could produce mis-timings so to check for this, I used independent component analyses (Beckmann & Smith, 2004) to analyse the data using a model-free approach. Because stimulation was designed in blocks of 45s of visual stimuli followed by 15s of fixation, ICA would be expected to extract one or more visual components following a similar time-course. Once again, in Participant #3 this was successful and showed a pattern similar to the model-based results in Figure 51. In the other two participants, however, no such components were identified suggesting a more fundamental issue with the data themselves.

All of the imaging data reported in the thesis to this point were collected using a modified Siemens 32-channel head coil. Specifically, the two channels around the eyes were removed because they often interfered with the participant's ability to read text. In other words, it is possible that the non-standard adjustment to the coil reduced the sensitivity of the coil and that this worsened, possibly dramatically, over time. The Katakana data were collected much later than then original data and moreover, participants' #1 and 4's data

were collected after Participant #3's. To test this, I re-ran participant #4 on a single run of the Katakana experiment using a standard Siemen's 12-channel head coil. Once again, the activations were weak with minimal activity in V1-V3 and nothing detected in vOT. This was true for English > fixation, Katakana > fixation, and All stimuli > fixation, suggesting that the problem may not have been due to a faulty head coil. As I was unable to identify, let alone correct, the source of the problem, I decided not to scan the fourth participant (#2) to avoid wasting her time.

Given only a single good data set, I compared the activation elicited by the English words relative to the Katakana strings in Participant #3 but there were no significant differences ($Z>1.96$). Indeed, the activation patterns for English > fixation and Katakana > fixation were very similar, providing no evidence that peripheral activation in V1-V3 was due to associated phonological or semantic information feeding back via top-down projections to the periphery. Obviously, this difference is a null result in a single participant and would be more compelling had I been able to test it in the other participants.

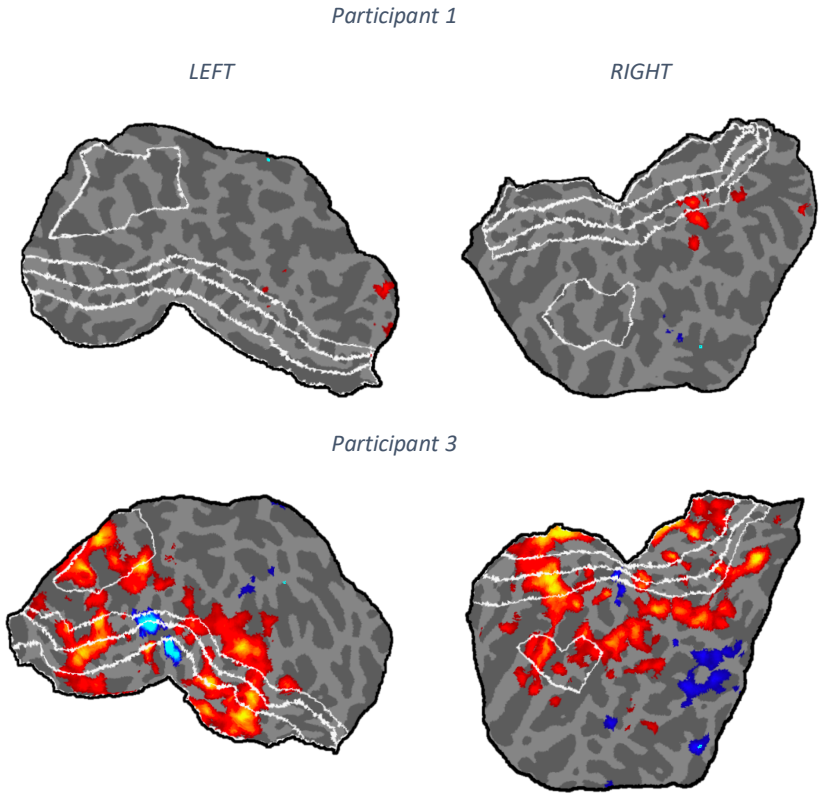


*Figure 51. Activation for the English > Rest contrast in the modified Katakana version of the covert reading task shown on the left and right occipital patches of the three participants that were scanned. As can be seen in Participants 1 and 4, there was conspicuously little activation in the early visual cortices (or elsewhere) and these results are dramatically different than their original covert reading results (see section 3.6.2). The data for Participant 3 however, is much more consistent with the original dataset. Scanning of Participant 2 was cancelled after the issue was detected.*

# Appendix B

## 1. Non-masked analysis

As mentioned in Chapter 6, there is more than one way to define early visual regions-of-interest. The approach I used throughout the thesis was to only consider voxels within an area (visual field map) that were 'active' above an arbitrary threshold (Z>2.3 for all the reported results although other thresholds were also tested). An alternative would be to treat an entire region as the ROI. For instance, the central regions of V1, V2, and V3 were those populations mapped to 0° to 3.8° – the region where visual stimuli would have appeared on the retina. Using this alternative ROI definition, I re-analysed the effects of stimuli on the central regions of the early visual cortices to determine whether this altered the results. Because vOT does not have a clear retinotopic organization, it was excluded from this analysis resulting in a 2 (Hemisphere) $\times$ 4 (Stimuli type) $\times$ 3 (Area: V1-V3) ANOVA with BOLD signal change in the central region the dependent measure. A significant main effect of Area [F(2,6)=6.339, p=0.033] confirmed decreasing activation from V1 (1.6%) to V2 (0.8%) to V3 (0.1%), as originally reported in Chapter 3. Unlike the original analysis, there was a significant main effect of Stimuli Type [F(2,6)=6.061, p=0.036] indicating that different stimulus conditions differentially affected activation in early visual cortices despite being closely matched on visual and orthographic properties. Specifically, low frequency words showed significantly greater activation than high frequency words [t(3)=4.880, p=0.016] across the early visual cortices (see Figure 52). In other words, in the earliest cortical regions coding visual stimuli, there was a significant difference in BOLD signal linked to lexical frequency. A final analysis looked at task effects specifically in the central regions of

the early visual areas and found a trend towards a main effect of Task [F(3,9)=3.330, p=0.070] but it was not significant and there were no significant interactions [all p>0.070], similar to the original results.

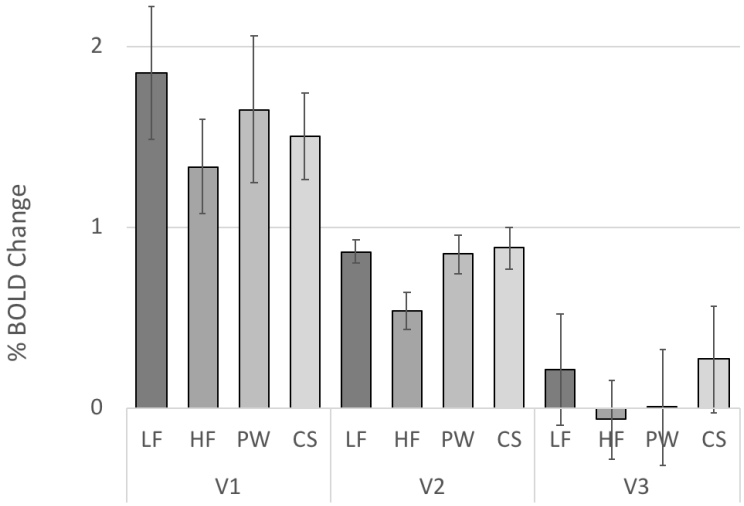


*Figure 52. Area effect size in the central ROI for each of the four conditions. Effect size was calculated across all the voxels in the ROI not just the those that exceeded threshold (Z>2.3).*

Obviously, altering the definition of the ROI can influence the results, at least for some analyses. Given the lack of a community-agreed 'gold standard' for how to define these regions, it is tempting to choose one that results in the most interesting findings. This, however, is a form of p-hacking that involves a post-hoc selection of findings and is not a valid method for deciding on the 'right' ROI definition. As a result, I chose a definition before conducting my analyses that seemed reasonable a priori, namely the active voxels within a region, and used it consistently in my analyses.

# Appendix C

## 1. English stimuli list

### *Consonant Strings*

| SET 1 | SET 2 | SET 3 | SET 4 | SET 5 |
|---|---|---|---|---|
| bznfj | bchl | bdxvv | cggf | bsff |
| cccvq | bhllj | bhrh | cgkr | bxrg |
| cchw | bnzqs | brbt | cxzq | dpkzr |
| cgsrw | brlq | cbhhw | dqzs | gcws |
| cslbt | csbl | cclcv | fdgsl | gssg |
| dsfd | czpcc | dfrm | fqkqq | gwgmk |
| gkcc | gxmv | gmcm | gflsv | hqscf |
| gmkcr | hhznz | gwsd | gsrlp | jjkqj |
| gzwm | jjxrp | hlncc | hqnvr | kwtbx |
| jrbr | jtmd | hqkg | jtsh | lczq |
| ldjjd | ldklg | jbgs | kbxm | lrqpr |
| lkrb | lksr | jczp | kcjtq | lrtb |
| lscs | lqltd | jgnsg | lqrpc | mglqs |
| lvcmz | mbwq | jlzws | mjlql | mlgl |
| nvmj | mnqx | kbzm | mlhxk | nmclz |

| | | | | |
|---|---|---|---|---|
| phdm | mwhd | mhws | ndhj | pbxb |
| ptkl | nfwq | mjhwb | nnsdw | phfqm |
| qgtq | nlcjf | ntlsq | nsvmb | pqgp |
| qtvbp | pdspp | pgrjs | rwmvs | pxfjm |
| qvfgb | prqtx | qfdx | sjzwk | pzzkb |
| qvsmr | pvfn | qzbw | tqzrq | qptgl |
| sfbn | rfmd | rdlls | vkwbg | qxnbr |
| sgwrq | rrkj | rdnvh | vlts | rjmq |
| smcw | rwjr | szfv | vzqjr | sngc |
| tjcrl | rxrz | vdzn | wjph | tnxsc |
| vxvcl | svww | vwmb | xhvj | wbdfb |
| wjfn | tqcgq | wslq | xrkf | xnzw |
| wlzd | tqvs | wvls | xvth | xqxj |
| wpqmp | wrmkw | xfszh | zghlt | zfpm |
| wqndj | xcxv | zvnkh | zjxg | ztwqw |

*Pseudowords*

| SET 1 | SET 2 | SET 3 | SET 4 | SET 5 |
|---|---|---|---|---|
| ubber | ardle | cafer | alner | bame |
| pone | bilm | calt | bave | blish |

| | | | | |
|---|---|---|---|---|
| brich | blonk | cate | bidge | brabe |
| bort | choin | chep | birsh | caval |
| vork | colk | crean | buly | cived |
| mest | fream | droin | cloan | cose |
| biss | hent | enly | coble | dack |
| flink | herv | fent | famel | dant |
| tiner | huste | freet | flaze | denk |
| surk | hyme | frig | glore | drome |
| fonk | lamn | goan | grend | flark |
| tawer | lind | hesty | kilk | fump |
| feart | loid | jeint | meef | herp |
| pany | lotch | kine | moad | liat |
| lomp | lunks | larm | molk | madle |
| bulp | merny | leam | okern | mose |
| loce | nove | lume | parl | peign |
| cavel | nuite | luver | pold | peste |
| lount | pell | prect | rost | quild |
| spunt | pero | quisk | scray | quinn |
| slout | reint | seak | seck | raim |

| | | | | |
|---|---|---|---|---|
| glode | sever | skear | slipe | rald |
| unike | stabe | slear | sone | resh |
| showl | tant | stoll | spoat | rigot |
| wath | timb | tody | spone | saist |
| wreap | towic | trife | twish | stane |
| dode | vust | vide | vell | threp |
| gloan | wern | vomes | yife | ulfer |
| runk | woil | walf | yomes | wamy |
| slord | wutch | wilk | yose | whap |

*Low Frequency Words*

| SET 1 | SET 2 | SET 3 | SET 4 | SET 5 |
|---|---|---|---|---|
| bland | bang | alley | acre | abode |
| booth | calf | amuse | adorn | boast |
| canoe | clove | bribe | bail | cider |
| cheat | crawl | comet | bake | cone |
| dent | flask | crow | blew | cork |
| fable | flood | dread | bunch | earn |
| flare | grief | feast | candy | ether |
| flee | gust | frown | cape | fork |

| | | | | |
|---|---|---|---|---|
| foil | heal | fury | cigar | gown |
| fore | lion | ghost | clash | grape |
| graph | lung | gravy | crook | grind |
| idle | menu | grove | crush | hail |
| lodge | nail | hush | dock | halt |
| navel | pork | lease | fairy | herb |
| nerve | roar | lever | flock | hose |
| pearl | scare | lone | frail | lemon |
| pint | scout | olive | frost | maker |
| rush | shiny | onion | haze | maze |
| rusty | slang | oven | lens | peach |
| sage | speck | pill | lime | peel |
| sauce | stale | prune | mouse | prey |
| shout | tack | scorn | nest | reap |
| sigh | thaw | shed | oath | reel |
| skate | tray | smash | punch | seal |
| steam | trim | sole | shoe | sleet |
| tank | trout | stake | stair | sour |
| tempt | vain | stump | stole | sting |

| | | | | |
|---|---|---|---|---|
| toll | whirl | toad | tame | tear |
| weep | wreck | toil | troop | trick |
| yawn | yell | womb | veal | wink |

*High Frequency Words*

| SET 1 | SET 2 | SET 3 | SET 4 | SET 5 |
|---|---|---|---|---|
| blood | beach | baby | area | alone |
| board | break | ball | birth | army |
| broad | call | base | cool | brain |
| case | cloth | cent | drink | bread |
| cost | court | chair | event | city |
| dream | death | coast | fast | crowd |
| earth | dress | deep | flesh | date |
| fall | duty | door | gone | empty |
| film | edge | dozen | heat | farm |
| form | hard | face | hold | fire |
| full | house | floor | note | green |
| horse | level | forth | phone | half |
| judge | mass | give | point | happy |
| line | meat | gold | poor | issue |

| | | | | |
|---|---|---|---|---|
| party | money | group | rough | loss |
| piece | page | hotel | rural | metal |
| play | paper | human | shop | music |
| scene | pass | iron | shot | news |
| ship | plan | life | size | night |
| skin | quiet | path | soil | nine |
| smoke | rain | queen | steel | pain |
| soft | rate | range | table | plant |
| sound | road | role | taste | rare |
| spot | scale | safe | teeth | rise |
| stop | seat | state | trial | site |
| unit | suit | think | water | sleep |
| urban | term | trip | white | sweet |
| voice | tree | used | wine | team |
| wide | uncle | whole | woman | thing |
| year | walk | world | youth | turn |

*Target words for Phonological Decisions Task*

| |
|---|
| chad |
| kenya |

| |
|---|
| iran |
| oman |
| qatar |
| iraq |
| guam |
| peru |
| syria |
| china |
| egypt |
| chile |
| cuba |
| togo |
| spain |
| italy |
| india |
| japan |
| laos |
| fiji |

*Target words for Semantic Decisions Task*

| |
|---|
| anew |
| bayou |
| blue |
| coup |
| debut |
| ensue |
| guru |
| haiku |
| igloo |
| imbue |
| lieu |
| menu |
| queue |
| renew |
| shrew |
| sinew |
| tatoo |
| unto |
| unto |

venue

## 2. Katakana stimuli list

| | | | | |
|---|---|---|---|---|
| カーテン | ドラント | レイアウ | ダイニン | カボレイ |
| ーライス | ストロボ | ランドセ | ヤモンド | トコウキ |
| クッショ | グリッシ | タラクテ | ィネーシ | ゴカゾイ |
| カスタム | キシブル | ホルモン | クトップ | エネゼマ |
| タマイズ | モクラシ | ジェンス | デザイン | トンチコ |
| サイバー | ッシング | テキスト | ノユカリ | カボレイ |
| デーンジ | エクスタ | ユーモラ | オイラン | ナスビユ |
| ドメイン | スタンド | ホログラ | タソガレ | ミレボハ |
| ノータッ | ラックス | ドライブ | テンボウ | カシコミ |
| レッシン | ォームラ | ハウジン | ノツオン | イピペバ |
| イースタ | ォルクロ | ホットド | タソガレ | ポヨエヒ |
| トランス | ギャップ | オードブ | テンボウ | ソヤツユ |
| スプレッ | テッセン | バットマ | タイマツ | シャキュ |
| ワンピー | ェネラル | ヒルサイ | キュウキ | ルツボソ |
| イコール | ジャンル | ハイクラ | ルツボシ | ガンジョ |
| クスプレ | イアント | ヘリコプ | マタタビ | キュウキ |
| スパート | ドーナツ | ヘッドラ | ツレヅレ | ヨソウペ |
| デイリー | バリズム | ハンドル | ソクバク | ュウュウ |
| キサイト | フィルタ | キャップ | ヨダレカ | イピカヤ |
| ドンキー | ゴーイン | ムエッグ | グセリラ | ヤマベュ |
| ダージリ | ディフェ | オールバ | リハクレ | メジフイ |
| イートイ | ハイセン | メンタリ | カレミフ | ナゴリジ |
| ファクタ | フルーツ | デザート | マタタビ | デロョメ |
| デカンタ | ロテスク | ドキュメ | ノユカリ | カヤアッ |
| ンタジア | ラウンド | イエット | ヨダレカ | ココラケ |
| ファミリ | ギャラテ | ダイアロ | ダワタシ | ソニバヤ |
| イベント | イダンス | ショナリ | ユソクイ | イタクシ |
| ンタジア | ドットコ | タシオン | ミシノベ | アロソヨ |
| ッション | ホールデ | アビタシ | カッレコ | ソバユヅ |
| エレクト | クラクシ | クトリィ | イチタク | カシコナ |

バノエズ　エージェ　コンテス　カプセル　ドバック
リテソヌ　チャージ　オープン　キャンペ　サインペ
イカンミ　クリアラ　クッキー　カマンベ　ロニクス
ソクバク　ラカルト　セレモニ　ルシウム　フィクシ
クネサヤ　チェンジ　アダプタ　ネックス　ドンマイ
タイマツ　バンスド　クッキン　アパート　ティバル
トネコウ　エージェ　カウンセ　ンティク　タープラ
グゴヌサ　ペタイザ　セリング　ルシウム　ンメント
テャドエ　カジュア　クラック　ーサラダ　ジャック
コマコラ　エアバッ　カルチャ　キャベツ　ラボラト
シドャコ　クリーン　ゴーサイ　ブッシュ　リナック
ツプャヤ　センチュ　キューブ　バルクメ　デコルテ
ャンポラ　リエイト　チャリテ　ナウンス　ファット
ワヤクャ　キャッシ　ライシス　ビルトイ　グジュア
オイラン　クロック　クラスト　ティック　ラインナ
ボレヤサ　チャンネ　ジットカ　ボーナス　レングス
ケッツウ　アダプタ　リーミィ　ウォシュ　ディスカ
メチャジ　シャレー　クリーム　ベストセ　ハーゲン
レブロメ　カタログ　カップル　ジョッキ　ガッツポ
アホウン　エアマッ　マチュア　ビーンズ　ドライン
アッケカ　ャッシュ　カテゴリ　ヨネット　イメート
ギパネイ　シュカー　クラシッ　メニティ　ドクター
ヤマベジ　キャッツ　セメント　ヨネット　デジタル
エグケト　クロゼト　アラーム　ッシュコ　イレクト
ソバユイ　カセット　ウンター　アダルト　マゾムグ
デミック　コーディ　チャット　プライズ　フッコカ
クセント　コインラ　ンション　リーディ　ボンチヤ
アクリル　メニティ　ュニティ　オキシン　ゲゾタチ
アカデミ　コレクシ　ンパクト　トンチコ　ボンチジ
ィビティ　セラミッ　カラメル　ヌンモイ　トコウキ